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(71) Applicant: CORIXA CORPORATION [US/US]; Suite 200, 1124 Columbia Street, Seattle, WA 98104 (US).			
(72) Inventors: REED, Steven, G.; 2843 - 122nd Place N.E., Bellevue, WA 98005 (US). LODES, Michael, J.; 9223 - 36th Avenue S.W., Seattle, WA 98126 (US). FRUDAKIS, Tony, N.; P.O. Box 99232, Seattle, WA 99232-0232 (US). MOHAMATH, Raodoh; 4205 South Morgan, Seattle, WA 98118 (US).			
(74) Agents: MAKI, David, J. et al.; Seed and Berry LLP, 6300 Columbia Center, 701 Fifth Avenue, Seattle, WA 98104-7092 (US).		Published <i>Without international search report and to be republished upon receipt of that report.</i>	

(54) Title: COMPOUNDS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER AND METHODS FOR THEIR USE

(57) Abstract

Compounds and methods for treating lung cancer are provided. The inventive compounds include polypeptides containing at least a portion of a lung tumor protein. Vaccines and pharmaceutical compositions for immunotherapy of lung cancer comprising such polypeptides, or polynucleotides encoding such polypeptides, are also provided, together with polynucleotides for preparing the inventive polypeptides.

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COMPOUNDS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER AND METHODS FOR THEIR USE

5 TECHNICAL FIELD

The present invention relates generally to compositions and methods for the treatment of lung cancer. The invention is more specifically related to nucleotide sequences that are preferentially expressed in lung tumor tissue, together with polypeptides encoded by such nucleotide sequences. The inventive nucleotide sequences and polypeptides may be used
10 in vaccines and pharmaceutical compositions for the treatment of lung cancer.

BACKGROUND OF THE INVENTION

Lung cancer is the primary cause of cancer death among both men and women in the U.S., with an estimated 172,000 new cases being reported in 1994. The five-year
15 survival rate among all lung cancer patients, regardless of the stage of disease at diagnosis, is only 13%. This contrasts with a five-year survival rate of 46% among cases detected while the disease is still localized. However, only 16% of lung cancers are discovered before the disease has spread.

Early detection is difficult since clinical symptoms are often not seen until the
20 disease has reached an advanced stage. Currently, diagnosis is aided by the use of chest x-rays, analysis of the type of cells contained in sputum and fiberoptic examination of the bronchial passages. Treatment regimens are determined by the type and stage of the cancer, and include surgery, radiation therapy and/or chemotherapy. In spite of considerable research into therapies for the disease, lung cancer remains difficult to treat.

25 Accordingly, there remains a need in the art for improved vaccines, treatment methods and diagnostic techniques for lung cancer.

SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compounds and methods for the
30 therapy of lung cancer. In a first aspect, isolated polynucleotides encoding lung tumor polypeptides are provided, such polynucleotides comprising a nucleotide sequence selected

from the group consisting of: (a) sequences provided in SEQ ID NO: 1-11, 19, 22-25, 27-31, 51, 53, 55, 63, 70, 72, 79, 80, 86, 87, 89, 90, 102-107, 109, 139, 143-149, 151-154 and 156-158; (b) sequences complementary to a sequence provided in SEQ ID NO: 1-11, 19, 22-25, 27-31, 51, 53, 55, 63, 70, 72, 79, 80, 86, 87, 89, 90, 102-107, 109, 139, 143-149, 151-154 and 156-158; and (b) variants of the sequences of (a) or (b).

In a second aspect, isolated polypeptides are provided that comprise at least an immunogenic portion of a lung tumor protein or a variant thereof. In specific embodiments, such polypeptides comprise an amino acid sequence encoded by a DNA sequence comprising a nucleotide sequence selected from the group consisting of (a) sequences recited in SEQ ID NO: 1-11, 19, 22-25, 27-31, 51, 53, 55, 63, 70, 72, 79, 80, 86, 87, 89, 90, 102-107, 109, 139, 143-149, 151-154 and 156-158; (b) sequences complementary to a sequence provided in SEQ ID NO: 1-11, 19, 22-25, 27-31, 51, 53, 55, 63, 70, 72, 79, 80, 86, 87, 89, 90, 102-107, 109, 139, 143-149, 151-154 and 156-158; and (c) variants of the sequences of (a) and (b).

In related aspects, expression vectors comprising the inventive polynucleotides, together with host cells transformed or transfected with such expression vectors are provided. In preferred embodiments, the host cells are selected from the group consisting of *E. coli*, yeast and mammalian cells.

In another aspect, fusion proteins comprising a first and a second inventive polypeptide or, alternatively, an inventive polypeptide and a known lung tumor antigen, are provided.

The present invention further provides pharmaceutical compositions comprising one or more of the above polypeptides, fusion proteins or polynucleotides and a physiologically acceptable carrier, together with vaccines comprising one or more such polypeptides, fusion proteins or polynucleotides in combination with an immune response enhancer.

In related aspects, the present invention provides methods for inhibiting the development of lung cancer in a patient, comprising administering to a patient an effective amount of at least one of the above pharmaceutical compositions and/or vaccines.

In yet a further aspect of the present invention, methods are provided for detecting lung cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that is capable of binding to a polypeptide disclosed

herein; and (b) detecting in the sample a protein or polypeptide that binds to the binding agent. In preferred embodiments, the binding agent is an antibody, most preferably a monoclonal antibody.

In related aspects, methods are provided for monitoring the progression of lung cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that is capable of binding to one of the polypeptides disclosed herein; (b) determining in the sample an amount of a protein or polypeptide that binds to the binding agent; (c) repeating steps (a) and (b); and comparing the amounts of polypeptide detected in steps (b) and (c).

Within related aspects, the present invention provides antibodies, preferably monoclonal antibodies, that bind to the inventive polypeptides, as well as diagnostic kits comprising such antibodies, and methods of using such antibodies to inhibit the development of lung cancer.

The present invention further provides methods for detecting lung cancer comprising: (a) obtaining a biological sample from a patient; (b) contacting the sample with a first and a second oligonucleotide primer in a polymerase chain reaction, at least one of the oligonucleotide primers being specific for a polynucleotide that encodes one of the polypeptides disclosed herein; and (c) detecting in the sample a DNA sequence that amplifies in the presence of the first and second oligonucleotide primers. In a preferred embodiment, at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of a polynucleotide comprising a sequence selected from the group consisting of SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181.

In a further aspect, the present invention provides a method for detecting lung cancer in a patient comprising: (a) obtaining a biological sample from the patient; (b) contacting the sample with an oligonucleotide probe specific for a polynucleotide that encodes one of the polypeptides disclosed herein; and (c) detecting in the sample a DNA sequence that hybridizes to the oligonucleotide probe. Preferably, the oligonucleotide probe comprises at least about 15 contiguous nucleotides of a polynucleotide comprising a sequence selected from the group consisting of SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181. In related aspects, diagnostic kits comprising the above oligonucleotide probes or primers are provided.

In yet a further aspect, methods for the treatment of lung cancer in a patient are provided, the methods comprising obtaining PBMC from the patient, incubating the PBMC with a polypeptide of the present invention (or a polynucleotide that encodes such a polypeptide) to provide incubated T cells and administering the incubated T cells to the patient. In present invention additionally provides methods for the treatment of lung cancer that comprise incubating antigen presenting cells with a polypeptide of the present invention (or a polynucleotide that encodes such a polypeptide) to provide incubated antigen presenting cells and administering the incubated antigen presenting cells to the patient. In certain embodiments, the antigen presenting cells are selected from the group consisting of dendritic cells and macrophages. Compositions for the treatment of lung cancer comprising T cells or antigen presenting cells that have been incubated with a polypeptide or polynucleotide of the present invention are also provided. These and other aspects of the present invention will become apparent upon reference to the following detailed description. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

SEQUENCE IDENTIFIERS

- SEQ ID NO: 1 is the determined cDNA sequence for L363C1.cons
SEQ ID NO: 2 is the determined cDNA sequence for L263C2.cons
20 SEQ ID NO: 3 is the determined cDNA sequence for L263C2c
SEQ ID NO: 4 is the determined cDNA sequence for L263C1.cons
SEQ ID NO: 5 is the determined cDNA sequence for L263C1b
SEQ ID NO: 6 is the determined cDNA sequence for L164C2.cons
SEQ ID NO: 7 is the determined cDNA sequence for L164C1.cons
25 SEQ ID NO: 8 is the determined cDNA sequence for L366C1a
SEQ ID NO: 9 is the determined cDNA sequence for L260C1.cons
SEQ ID NO: 10 is the determined cDNA sequence for L163C1c
SEQ ID NO: 11 is the determined cDNA sequence for L163C1b
SEQ ID NO: 12 is the determined cDNA sequence for L255C1.cons
30 SEQ ID NO: 13 is the determined cDNA sequence for L255C1b

- SEQ ID NO: 14 is the determined cDNA sequence for L355C1.cons
SEQ ID NO: 15 is the determined cDNA sequence for L366C1.cons
SEQ ID NO: 16 is the determined cDNA sequence for L163C1a
SEQ ID NO: 17 is the determined cDNA sequence for LT86-1
5 SEQ ID NO: 18 is the determined cDNA sequence for LT86-2
SEQ ID NO: 19 is the determined cDNA sequence for LT86-3
SEQ ID NO: 20 is the determined cDNA sequence for LT86-4
SEQ ID NO: 21 is the determined cDNA sequence for LT86-5
SEQ ID NO: 22 is the determined cDNA sequence for LT86-6
10 SEQ ID NO: 23 is the determined cDNA sequence for LT86-7
SEQ ID NO: 24 is the determined cDNA sequence for LT86-8
SEQ ID NO: 25 is the determined cDNA sequence for LT86-9
SEQ ID NO: 26 is the determined cDNA sequence for LT86-10
SEQ ID NO: 27 is the determined cDNA sequence for LT86-11
15 SEQ ID NO: 28 is the determined cDNA sequence for LT86-12
SEQ ID NO: 29 is the determined cDNA sequence for LT86-13
SEQ ID NO: 30 is the determined cDNA sequence for LT86-14
SEQ ID NO: 31 is the determined cDNA sequence for LT86-15
SEQ ID NO: 32 is the predicted amino acid sequence for LT86-1
20 SEQ ID NO: 33 is the predicted amino acid sequence for LT86-2
SEQ ID NO: 34 is the predicted amino acid sequence for LT86-3
SEQ ID NO: 35 is the predicted amino acid sequence for LT86-4
SEQ ID NO: 36 is the predicted amino acid sequence for LT86-5
SEQ ID NO: 37 is the predicted amino acid sequence for LT86-6
25 SEQ ID NO: 38 is the predicted amino acid sequence for LT86-7
SEQ ID NO: 39 is the predicted amino acid sequence for LT86-8
SEQ ID NO: 40 is the predicted amino acid sequence for LT86-9
SEQ ID NO: 41 is the predicted amino acid sequence for LT86-10
SEQ ID NO: 42 is the predicted amino acid sequence for LT86-11
30 SEQ ID NO: 43 is the predicted amino acid sequence for LT86-12

- SEQ ID NO: 44 is the predicted amino acid sequence for LT86-13
SEQ ID NO: 45 is the predicted amino acid sequence for LT86-14
SEQ ID NO: 46 is the predicted amino acid sequence for LT86-15
SEQ ID NO: 47 is a (dT)₁₂AG primer
- 5 SEQ ID NO: 48 is a primer
SEQ ID NO: 49 is the determined 5' cDNA sequence for L86S-3
SEQ ID NO: 50 is the determined 5' cDNA sequence for L86S-12
SEQ ID NO: 51 is the determined 5' cDNA sequence for L86S-16
SEQ ID NO: 52 is the determined 5' cDNA sequence for L86S-25
- 10 SEQ ID NO: 53 is the determined 5' cDNA sequence for L86S-36
SEQ ID NO: 54 is the determined 5' cDNA sequence for L86S-40
SEQ ID NO: 55 is the determined 5' cDNA sequence for L86S-46
SEQ ID NO: 56 is the predicted amino acid sequence for L86S-3
SEQ ID NO: 57 is the predicted amino acid sequence for L86S-12
- 15 SEQ ID NO: 58 is the predicted amino acid sequence for L86S-16
SEQ ID NO: 59 is the predicted amino acid sequence for L86S-25
SEQ ID NO: 60 is the predicted amino acid sequence for L86S-36
SEQ ID NO: 61 is the predicted amino acid sequence for L86S-40
SEQ ID NO: 62 is the predicted amino acid sequence for L86S-46
- 20 SEQ ID NO: 63 is the determined 5' cDNA sequence for L86S-30
SEQ ID NO: 64 is the determined 5' cDNA sequence for L86S-41
SEQ ID NO: 65 is the predicted amino acid sequence from the 5' end of LT86-9
SEQ ID NO: 66 is the determined extended cDNA sequence for LT86-4
SEQ ID NO: 67 is the predicted extended amino acid sequence for LT86-4
- 25 SEQ ID NO: 68 is the determined 5' cDNA sequence for LT86-20
SEQ ID NO: 69 is the determined 3' cDNA sequence for LT86-21
SEQ ID NO: 70 is the determined 5' cDNA sequence for LT86-22
SEQ ID NO: 71 is the determined 5' cDNA sequence for LT86-26
SEQ ID NO: 72 is the determined 5' cDNA sequence for LT86-27
- 30 SEQ ID NO: 73 is the predicted amino acid sequence for LT86-20

- SEQ ID NO: 74 is the predicted amino acid sequence for LT86-21
SEQ ID NO: 75 is the predicted amino acid sequence for LT86-22
SEQ ID NO: 76 is the predicted amino acid sequence for LT86-26
SEQ ID NO: 77 is the predicted amino acid sequence for LT86-27
5 SEQ ID NO: 78 is the determined extended cDNA sequence for L86S-12
SEQ ID NO: 79 is the determined extended cDNA sequence for L86S-36
SEQ ID NO: 80 is the determined extended cDNA sequence for L86S-46
SEQ ID NO: 81 is the predicted extended amino acid sequence for L86S-12
SEQ ID NO: 82 is the predicted extended amino acid sequence for L86S-36
10 SEQ ID NO: 83 is the predicted extended amino acid sequence for L86S-46
SEQ ID NO: 84 is the determined 5'cDNA sequence for L86S-6
SEQ ID NO: 85 is the determined 5'cDNA sequence for L86S-11
SEQ ID NO: 86 is the determined 5'cDNA sequence for L86S-14
SEQ ID NO: 87 is the determined 5'cDNA sequence for L86S-29
15 SEQ ID NO: 88 is the determined 5'cDNA sequence for L86S-34
SEQ ID NO: 89 is the determined 5'cDNA sequence for L86S-39
SEQ ID NO: 90 is the determined 5'cDNA sequence for L86S-47
SEQ ID NO: 91 is the determined 5'cDNA sequence for L86S-49
SEQ ID NO: 92 is the determined 5'cDNA sequence for L86S-51
20 ~~SEQ ID NO: 93 is the predicted amino acid sequence for L86S-6~~
SEQ ID NO: 94 is the predicted amino acid sequence for L86S-11
SEQ ID NO: 95 is the predicted amino acid sequence for L86S-14
SEQ ID NO: 96 is the predicted amino acid sequence for L86S-29
SEQ ID NO: 97 is the predicted amino acid sequence for L86S-34
25 SEQ ID NO: 98 is the predicted amino acid sequence for L86S-39
SEQ ID NO: 99 is the predicted amino acid sequence for L86S-47
SEQ ID NO: 100 is the predicted amino acid sequence for L86S-49
SEQ ID NO: 101 is the predicted amino acid sequence for L86S-51
SEQ ID NO: 102 is the determined DNA sequence for SLT-T1
30 SEQ ID NO: 103 is the determined 5' cDNA sequence for SLT-T2

- SEQ ID NO: 104 is the determined 5' cDNA sequence for SLT-T3
SEQ ID NO: 105 is the determined 5' cDNA sequence for SLT-T5
SEQ ID NO: 106 is the determined 5' cDNA sequence for SLT-T7
SEQ ID NO: 107 is the determined 5' cDNA sequence for SLT-T9
5 SEQ ID NO: 108 is the determined 5' cDNA sequence for SLT-T10
SEQ ID NO: 109 is the determined 5' cDNA sequence for SLT-T11
SEQ ID NO: 110 is the determined 5' cDNA sequence for SLT-T12
SEQ ID NO: 111 is the predicted amino acid sequence for SLT-T1
SEQ ID NO: 112 is the predicted amino acid sequence for SLT-T2
10 SEQ ID NO: 113 is the predicted amino acid sequence for SLT-T3
SEQ ID NO: 114 is the predicted amino acid sequence for SLT-T10
SEQ ID NO: 115 is the predicted amino acid sequence for SLT-T12
SEQ ID NO: 116 is the determined 5' cDNA sequence for SALT-T3
SEQ ID NO: 117 is the determined 5' cDNA sequence for SALT-T4
15 SEQ ID NO: 118 is the determined 5' cDNA sequence for SALT-T7
SEQ ID NO: 119 is the determined 5' cDNA sequence for SALT-T8
SEQ ID NO: 120 is the determined 5' cDNA sequence for SALT-T9
SEQ ID NO: 121 is the predicted amino acid sequence for SALT-T3
SEQ ID NO: 122 is the predicted amino acid sequence for SALT-T4
20 SEQ ID NO: 123 is the predicted amino acid sequence for SALT-T7
SEQ ID NO: 124 is the predicted amino acid sequence for SALT-T8
SEQ ID NO: 125 is the predicted amino acid sequence for SALT-T9
SEQ ID NO: 126 is the determined cDNA sequence for PSLT-1
SEQ ID NO: 127 is the determined cDNA sequence for PSLT-2
25 SEQ ID NO: 128 is the determined cDNA sequence for PSLT-7
SEQ ID NO: 129 is the determined cDNA sequence for PSLT-13
SEQ ID NO: 130 is the determined cDNA sequence for PSLT-27
SEQ ID NO: 131 is the determined cDNA sequence for PSLT-28
SEQ ID NO: 132 is the determined cDNA sequence for PSLT-30
30 SEQ ID NO: 133 is the determined cDNA sequence for PSLT-40

- SEQ ID NO: 134 is the determined cDNA sequence for PSLT-69
SEQ ID NO: 135 is the determined cDNA sequence for PSLT-71
SEQ ID NO: 136 is the determined cDNA sequence for PSLT-73
SEQ ID NO: 137 is the determined cDNA sequence for PSLT-79
5 SEQ ID NO: 138 is the determined cDNA sequence for PSLT-03
SEQ ID NO: 139 is the determined cDNA sequence for PSLT-09
SEQ ID NO: 140 is the determined cDNA sequence for PSLT-011
SEQ ID NO: 141 is the determined cDNA sequence for PSLT-041
SEQ ID NO: 142 is the determined cDNA sequence for PSLT-62
10 SEQ ID NO: 143 is the determined cDNA sequence for PSLT-6
SEQ ID NO: 144 is the determined cDNA sequence for PSLT-37
SEQ ID NO: 145 is the determined cDNA sequence for PSLT-74
SEQ ID NO: 146 is the determined cDNA sequence for PSLT-010
SEQ ID NO: 147 is the determined cDNA sequence for PSLT-012
15 SEQ ID NO: 148 is the determined cDNA sequence for PSLT-037
SEQ ID NO: 149 is the determined 5' cDNA sequence for SAL-3
SEQ ID NO: 150 is the determined 5' cDNA sequence for SAL-24
SEQ ID NO: 151 is the determined 5' cDNA sequence for SAL-25
SEQ ID NO: 152 is the determined 5' cDNA sequence for SAL-33
20 SEQ ID NO: 153 is the determined 5' cDNA sequence for SAL-50
SEQ ID NO: 154 is the determined 5' cDNA sequence for SAL-57
SEQ ID NO: 155 is the determined 5' cDNA sequence for SAL-66
SEQ ID NO: 156 is the determined 5' cDNA sequence for SAL-82
SEQ ID NO: 157 is the determined 5' cDNA sequence for SAL-99
25 SEQ ID NO: 158 is the determined 5' cDNA sequence for SAL-104
SEQ ID NO: 159 is the determined 5' cDNA sequence for SAL-109
SEQ ID NO: 160 is the determined 5' cDNA sequence for SAL-5
SEQ ID NO: 161 is the determined 5' cDNA sequence for SAL-8
SEQ ID NO: 162 is the determined 5' cDNA sequence for SAL-12
30 SEQ ID NO: 163 is the determined 5' cDNA sequence for SAL-14

- SEQ ID NO: 164 is the determined 5' cDNA sequence for SAL-16
SEQ ID NO: 165 is the determined 5' cDNA sequence for SAL-23
SEQ ID NO: 166 is the determined 5' cDNA sequence for SAL-26
SEQ ID NO: 167 is the determined 5' cDNA sequence for SAL-29
5 SEQ ID NO: 168 is the determined 5' cDNA sequence for SAL-32
SEQ ID NO: 169 is the determined 5' cDNA sequence for SAL-39
SEQ ID NO: 170 is the determined 5' cDNA sequence for SAL-42
SEQ ID NO: 171 is the determined 5' cDNA sequence for SAL-43
SEQ ID NO: 172 is the determined 5' cDNA sequence for SAL-44
10 SEQ ID NO: 173 is the determined 5' cDNA sequence for SAL-48
SEQ ID NO: 174 is the determined 5' cDNA sequence for SAL-68
SEQ ID NO: 175 is the determined 5' cDNA sequence for SAL-72
SEQ ID NO: 176 is the determined 5' cDNA sequence for SAL-77
SEQ ID NO: 177 is the determined 5' cDNA sequence for SAL-86
15 SEQ ID NO: 178 is the determined 5' cDNA sequence for SAL-88
SEQ ID NO: 179 is the determined 5' cDNA sequence for SAL-93
SEQ ID NO: 180 is the determined 5' cDNA sequence for SAL-100
SEQ ID NO: 181 is the determined 5' cDNA sequence for SAL-105
SEQ ID NO: 182 is the predicted amino acid sequence for SAL-3
20 SEQ ID NO: 183 is the predicted amino acid sequence for SAL-24
SEQ ID NO: 184 is a first predicted amino acid sequence for SAL-25
SEQ ID NO: 185 is a second predicted amino acid sequence for SAL-25
SEQ ID NO: 186 is the predicted amino acid sequence for SAL-33
SEQ ID NO: 187 is a first predicted amino acid sequence for SAL-50
25 SEQ ID NO: 188 is the predicted amino acid sequence for SAL-57
SEQ ID NO: 189 is a first predicted amino acid sequence for SAL-66
SEQ ID NO: 190 is a second predicted amino acid sequence for SAL-66
SEQ ID NO: 191 is the predicted amino acid sequence for SAL-82
SEQ ID NO: 192 is the predicted amino acid sequence for SAL-99
30 SEQ ID NO: 193 is the predicted amino acid sequence for SAL-104

- SEQ ID NO: 194 is the predicted amino acid sequence for SAL-5
SEQ ID NO: 195 is the predicted amino acid sequence for SAL-8
SEQ ID NO: 196 is the predicted amino acid sequence for SAL-12
SEQ ID NO: 197 is the predicted amino acid sequence for SAL-14
5 SEQ ID NO: 198 is the predicted amino acid sequence for SAL-16
SEQ ID NO: 199 is the predicted amino acid sequence for SAL-23
SEQ ID NO: 200 is the predicted amino acid sequence for SAL-26
SEQ ID NO: 201 is the predicted amino acid sequence for SAL-29
SEQ ID NO: 202 is the predicted amino acid sequence for SAL-32
10 SEQ ID NO: 203 is the predicted amino acid sequence for SAL-39
SEQ ID NO: 204 is the predicted amino acid sequence for SAL-42
SEQ ID NO: 205 is the predicted amino acid sequence for SAL-43
SEQ ID NO: 206 is the predicted amino acid sequence for SAL-44
SEQ ID NO: 207 is the predicted amino acid sequence for SAL-48
15 SEQ ID NO: 208 is the predicted amino acid sequence for SAL-68
SEQ ID NO: 209 is the predicted amino acid sequence for SAL-72
SEQ ID NO: 210 is the predicted amino acid sequence for SAL-77
SEQ ID NO: 211 is the predicted amino acid sequence for SAL-86
SEQ ID NO: 212 is the predicted amino acid sequence for SAL-88
20 SEQ ID NO: 213 is the predicted amino acid sequence for SAL-93
SEQ ID NO: 214 is the predicted amino acid sequence for SAL-100
SEQ ID NO: 215 is the predicted amino acid sequence for SAL-105
SEQ ID NO: 216 is a second predicted amino acid sequence for SAL-50

25 DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy of lung cancer. The compositions described herein include polypeptides, fusion proteins and polynucleotides. Also included within the present invention are molecules (such as an antibody or fragment thereof) that bind to the inventive
30 polypeptides. Such molecules are referred to herein as "binding agents."

In one embodiment, the inventive polypeptides comprise at least a portion of a protein that is expressed at a greater level in human lung tumor tissue than in normal lung tissue. Preferably, the level of RNA encoding the polypeptide is at least 2-fold higher in tumor tissue. Such polypeptides include, but are not limited to, polypeptides (and immunogenic portions thereof) encoded by the nucleotide sequences provided in SEQ ID NO: 1-16 and variants thereof.

In a second embodiment, the inventive polypeptides comprise at least a portion of a immunogenic lung tumor protein, including but not limited to polypeptides wherein the lung tumor protein includes an amino acid sequence encoded by a polynucleotide including a sequence selected from the group consisting of (a) nucleotide sequences recited in SEQ ID NO: 17-31, 49-55, 63,64, 66, 68-72, 78-80 and 84-92, (b) the complements of said nucleotide sequences, and (c) variants of such sequences.

In a third embodiment, the inventive polypeptides comprise at least a portion of a lung tumor protein, including polypeptides wherein the lung tumor protein includes an amino acid sequence encoded by a polynucleotide including a sequence selected from the group consisting of (a) nucleotide sequences recited in SEQ ID NO: 102-110, 116-120 and 126-181, (b) the complements of said nucleotide sequences, and (c) variants of such sequences.

As used herein, the term "polypeptide" encompasses amino acid chains of any length, including full length proteins, wherein the amino acid residues are linked by covalent peptide bonds. Thus, a polypeptide comprising a portion of one of the above lung tumor proteins may consist entirely of the portion, or the portion may be present within a larger polypeptide that contains additional sequences. The additional sequences may be derived from the native protein or may be heterologous, and such sequences may (but need not) be immunoreactive and/or antigenic. As detailed below, such polypeptides may be isolated from lung tumor tissue or prepared by synthetic or recombinant means.

As used herein, an "immunogenic portion" of a lung tumor protein is a portion that is capable of eliciting an immune response in a patient inflicted with lung cancer and as such binds to antibodies present within sera from a lung cancer patient. Such immunogenic portions generally comprise at least about 5 amino acid residues, more preferably at least about 10, and most preferably at least about 20 amino acid residues. Immunogenic portions

of the proteins described herein may be identified in antibody binding assays. Such assays may generally be performed using any of a variety of means known to those of ordinary skill in the art, as described, for example, in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1988. For example, a polypeptide
5 may be immobilized on a solid support (as described below) and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ^{125}I -labeled Protein A. Alternatively, a polypeptide may be used to generate monoclonal and polyclonal
10 antibodies for use in detection of the polypeptide in blood or other fluids of lung cancer patients. Methods for preparing and identifying immunogenic portions of antigens of known sequence are well known in the art and include those summarized in Paul, *Fundamental Immunology*, 3rd ed., Raven Press, 1993, pp. 243-247.

The term "polynucleotide(s)," as used herein, means a single or double-stranded polymer of deoxyribonucleotide or ribonucleotide bases and includes DNA and
15 corresponding RNA molecules, including HnRNA and mRNA molecules, both sense and anti-sense strands, and comprehends cDNA, genomic DNA and recombinant DNA, as well as wholly or partially synthesized polynucleotides. An HnRNA molecule contains introns and corresponds to a DNA molecule in a generally one-to-one manner. An mRNA molecule
20 corresponds to an HnRNA and DNA molecule from which the introns have been excised. A polynucleotide may consist of an entire gene, or any portion thereof. Operable anti-sense polynucleotides may comprise a fragment of the corresponding polynucleotide, and the definition of "polynucleotide" therefore includes all such operable anti-sense fragments.

The compositions and methods of the present invention also encompass variants of the above polypeptides and polynucleotides.

25 A polypeptide "variant," as used herein, is a polypeptide that differs from the recited polypeptide only in conservative substitutions and/or modifications, such that the antigenic properties of the polypeptide are retained. In a preferred embodiment, variant polypeptides differ from an identified sequence by substitution, deletion or addition of five amino acids or fewer. Such variants may generally be identified by modifying one of the
30 above polypeptide sequences, and evaluating the antigenic properties of the modified polypeptide using, for example, the representative procedures described herein. Polypeptide

variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described below) to the identified polypeptides.

As used herein, a "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties. such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophobic nature of the polypeptide to be substantially unchanged. In general, the following groups of amino acids represent conservative changes: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his.

Variants may also, or alternatively, contain other modifications, including the deletion or addition of amino acids that have minimal influence on the antigenic properties, secondary structure and hydrophobic nature of the polypeptide. For example, a polypeptide may be conjugated to a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (*e.g.*, poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

A nucleotide "variant" is a sequence that differs from the recited nucleotide sequence in having one or more nucleotide deletions, substitutions or additions. Such modifications may be readily introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis as taught, for example, by Adelman et al. (*DNA*, 2:183, 1983). Nucleotide variants may be naturally occurring allelic variants, or non-naturally occurring variants. Variant nucleotide sequences preferably exhibit at least about 70%, more preferably at least about 80% and most preferably at least about 90% identity (determined as described below) to the recited sequence.

The lung tumor antigens provided by the present invention include variants that are encoded by DNA sequences which are substantially homologous to one or more of the DNA sequences specifically recited herein. "Substantial homology," as used herein, refers to DNA sequences that are capable of hybridizing under moderately stringent conditions. Suitable moderately stringent conditions include prewashing in a solution of 5X

SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5X SSC, overnight or, in the event of cross-species homology, at 45°C with 0.5X SSC; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS. Such hybridizing DNA sequences are also within the scope of this invention, as are nucleotide
5 sequences that, due to code degeneracy, encode an immunogenic polypeptide that is encoded by a hybridizing DNA sequence.

Two nucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acid residues in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are
10 typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

15 Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of*
20 *Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5; Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) Fast and sensitive multiple sequence alignments on a microcomputer *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) Optimal alignments
25 in linear space *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) The neighbor joining method. A new method for reconstructing phylogenetic trees *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) Rapid similarity searches of nucleic
30 acid and protein data banks *Proc. Natl. Acad. Sci. USA* 80:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (i.e. gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e. the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

The lung tumor polypeptides of the present invention, and polynucleotides encoding such polypeptides, may be isolated from lung tumor tissue using any of a variety of methods well known in the art. For example, cDNA molecules encoding polypeptides preferentially expressed in lung tumor tissue may be cloned on the basis of the lung tumor-specific expression of the corresponding mRNAs, using differential display PCR. This technique compares the amplified products from RNA templates prepared from normal lung and lung tumor tissue. cDNA may be prepared by reverse transcription of RNA using a (dT)₁₂AG primer. Following amplification of the cDNA using a random primer, a band corresponding to an amplified product specific to the tumor RNA may be cut out from a silver stained gel and subcloned into a suitable vector. Examples of cDNA sequences that may be isolated using this procedure include those provided in SEQ ID NO: 1-16.

cDNA molecules encoding immunogenic lung tumor polypeptides may be prepared by screening a cDNA expression library prepared from a lung tumor sample with sera from the same patient as the tumor sample, as described in detail in Example 2 below. Examples of cDNA sequences that may be isolated using this procedure include those provided in SEQ ID NO: 17-31. Additional cDNA molecules encoding lung tumor polypeptides may be obtained by screening such a cDNA expression library with mouse anti-lung tumor serum as described below in Example 3. Examples of cDNA sequences that may thus be isolated are provided in SEQ ID NO: 49-55, 63, 64 and 126-148. cDNA sequences encoding lung tumor antigens may also be isolated by screening of lung tumor cDNA

libraries prepared from SCID mice with mouse anti-tumor sera, as described below in Example 4. Examples of cDNA sequences that may be isolated using this technique are provided in SEQ ID NO: 149-181.

5 A gene encoding a polypeptide described herein (or a portion thereof) may, alternatively, be amplified from human genomic DNA, or from lung tumor cDNA, via polymerase chain reaction. For this approach, sequence-specific primers may be designed based on the nucleotide sequences provided herein and may be purchased or synthesized. An amplified portion of a specific nucleotide sequence may then be used to isolate the full length gene from a human genomic DNA library or from a lung tumor cDNA library, using well
10 known techniques, such as those described in Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY (1989).

Once a DNA sequence encoding a polypeptide is obtained, the polypeptide may be produced recombinantly by inserting the DNA sequence into an expression vector and expressing the polypeptide in an appropriate host. Any of a variety of expression vectors
15 known to those of ordinary skill in the art may be employed to express recombinant polypeptides of this invention. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a polynucleotide that encodes the recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian
20 cell line, such as COS or CHO cells. The DNA sequences expressed in this manner may encode naturally occurring polypeptides, portions of naturally occurring polypeptides, or other variants thereof. Supernatants from suitable host/vector systems which secrete the recombinant polypeptide may be first concentrated using a commercially available filter. The concentrate may then be applied to a suitable purification matrix, such as an affinity matrix or
25 ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify the recombinant polypeptide.

Such techniques may also be used to prepare polypeptides comprising portions or variants of the native polypeptides. Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may be generated using
30 techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as

the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain (see, for example, Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963). Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be
5 operated according to the manufacturer's instructions.

In general, regardless of the method of preparation, the polypeptides disclosed herein are prepared in an isolated, substantially pure form (*i.e.*, the polypeptides are homogenous as determined by amino acid composition and primary sequence analysis). Preferably, the polypeptides are at least about 90% pure, more preferably at least about 95%
10 pure and most preferably at least about 99% pure. In certain preferred embodiments, described in more detail below, the substantially pure polypeptides are incorporated into pharmaceutical compositions or vaccines for use in one or more of the methods disclosed herein.

In a related aspect, the present invention provides fusion proteins comprising a
15 first and a second inventive polypeptide or, alternatively, a polypeptide of the present invention and a known lung tumor antigen, together with variants of such fusion proteins. The fusion proteins of the present invention may (but need not) include a linker peptide between the first and second polypeptides.

A DNA sequence encoding a fusion protein of the present invention is
20 constructed using known recombinant DNA techniques to assemble separate DNA sequences encoding the first and second polypeptides into an appropriate expression vector. The 3' end of a DNA sequence encoding the first polypeptide is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide so that the reading frames of the sequences are in phase to permit mRNA translation of the two DNA sequences into a
25 single fusion protein that retains the biological activity of both the first and the second polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptides by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the
30 fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible

extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may be from 1 to about 50 amino acids in length. Peptide sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons require to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (see, for example, Stoute et al. *New Engl. J. Med.*, 336:86-91 (1997)).

Polypeptides that comprise an immunogenic portion of a lung tumor protein may generally be used for therapy of lung cancer, wherein the polypeptide stimulates the patient's own immune response to lung tumor cells. The present invention thus provides methods for using one or more of the compounds described herein (which may be polypeptides, polynucleotides or fusion proteins) for immunotherapy of lung cancer in a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may be afflicted with disease, or may be free of detectable disease. Accordingly, the compounds disclosed herein may be used to treat lung cancer or to inhibit the development of lung cancer. In a preferred embodiment, the compounds are administered

either prior to or following surgical removal of primary tumors and/or treatment by administration of radiotherapy and conventional chemotherapeutic drugs.

In these aspects, the inventive polypeptide is generally present within a pharmaceutical composition or a vaccine. Pharmaceutical compositions may comprise one or more polypeptides, each of which may contain one or more of the above sequences (or variants thereof), and a physiologically acceptable carrier. The vaccines may comprise one or more such polypeptides and an immune response enhancer, such as an adjuvant, biodegradable microsphere (e.g., polylactic galactide) or a liposome (into which the polypeptide is incorporated). Pharmaceutical compositions and vaccines may also contain other epitopes of lung tumor antigens, either incorporated into a fusion protein as described above (i.e., a single polypeptide that contains multiple epitopes) or present within a separate polypeptide.

Alternatively, a pharmaceutical composition or vaccine may contain DNA encoding one or more of the above polypeptides and/or fusion proteins, such that the polypeptide is generated *in situ*. In such pharmaceutical compositions and vaccines, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an epitope of a lung cell antigen on its cell surface. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *PNAS* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *PNAS* 91:215-219, 1994; Kass-Eisler et al., *PNAS* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of

ordinary skill in the art. The DNA may also be "naked," as described, for example, in published PCT application WO 90/11092, and Ulmer et al., *Science* 259:1745-1749, 1993, reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported
5 into the cells.

Routes and frequency of administration, as well as dosage, will vary from individual to individual and may parallel those currently being used in immunotherapy of other diseases. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous),
10 intranasally (*e.g.*, by aspiration) or orally. Between 1 and 10 doses may be administered over a 3-24 week period. Preferably, 4 doses are administered, at an interval of 3 months, and booster administrations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of polypeptide or DNA that is effective to raise an immune response (cellular and/or humoral) against lung tumor cells in
15 a treated patient. A suitable immune response is at least 10-50% above the basal (*i.e.*, untreated) level. In general, the amount of polypeptide present in a dose (or produced *in situ* by the DNA in a dose) ranges from about 1 pg to about 100 mg per kg of host, typically from about 10 pg to about 1 mg, and preferably from about 100 pg to about 1 μ g. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.01 mL to
20 about 5 mL.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a lipid, a wax
25 and/or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and/or magnesium carbonate, may be employed. Biodegradable microspheres (*e.g.*, polylactic glycolide) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S.
30 Patent Nos. 4,897,268 and 5,075,109.

Any of a variety of immune response enhancers may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a nonspecific stimulator of immune response, such as lipid A, *Bordella pertussis* or *Mycobacterium tuberculosis*. Such adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI), and Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ).

Within certain embodiments, polynucleotides of the present invention may be formulated so as to permit entry into a cell of a mammal, preferably a human, and expression therein. Such formulations are particularly useful for therapeutic purposes. Those of skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cells, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g. avian pox virus). Techniques for incorporating DNA into such vectors are well known to those of skill in the art. A retroviral vector may additionally transfer or incorporate a targeting moiety, such as a gene that encodes for a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Polypeptides disclosed herein may also be employed in adoptive immunotherapy for the treatment of cancer. Adoptive immunotherapy may be broadly classified into either active or passive immunotherapy. In active immunotherapy, treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (for example, tumor vaccines, bacterial adjuvants, and/or cytokines).

In passive immunotherapy, treatment involves the delivery of biologic reagents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T lymphocytes (for example, CD8+ cytotoxic T-lymphocyte, CD4+ T-helper, tumor-infiltrating lymphocytes), killer cells

(Natural Killer cells, lymphokine-activated killer cells), B cells, or antigen presenting cells (such as dendritic cells and macrophages) expressing the disclosed antigens. The polypeptides disclosed herein may also be used to generate antibodies or anti-idiotypic antibodies (as in U.S. Patent No. 4,918,164), for passive immunotherapy.

5 The predominant method of procuring adequate numbers of T-cells for adoptive immunotherapy is to grow immune T-cells *in vitro*. Culture conditions for expanding single antigen-specific T-cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. These *in vitro* culture conditions typically utilize intermittent stimulation with antigen, often in the presence of cytokines, such
10 as IL-2, and non-dividing feeder cells. As noted above, the immunoreactive polypeptides described herein may be used to rapidly expand antigen-specific T cell cultures in order to generate sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage or B-cells, may be pulsed with immunoreactive polypeptides or transfected with a polynucleotide sequence(s), using standard techniques well
15 known in the art. For cultured T-cells to be effective in therapy, the cultured T-cells must be able to grow and distribute widely and to survive long term *in vivo*. Studies have demonstrated that cultured T-cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever et al. *Ibid*).

20 ~~The polypeptides disclosed herein may also be employed to generate and/or~~
isolate tumor-reactive T-cells, which can then be administered to the patient. In one technique, antigen-specific T-cell lines may be generated by *in vivo* immunization with short peptides corresponding to immunogenic portions of the disclosed polypeptides. The resulting antigen specific CD8+ CTL clones may be isolated from the patient, expanded using standard
25 tissue culture techniques, and returned to the patient.

 Alternatively, peptides corresponding to immunogenic portions of the polypeptides may be employed to generate tumor reactive T cell subsets by selective *in vitro* stimulation and expansion of autologous T cells to provide antigen-specific T cells which may be subsequently transferred to the patient as described, for example, by Chang et al.
30 (*Crit. Rev. Oncol. Hematol.* 22(3), 213, 1996).

In another embodiment, syngeneic or autologous dendritic cells may be pulsed with peptides corresponding to at least an immunogenic portion of a polypeptide disclosed herein. The resulting antigen-specific dendritic cells may either be transferred into a patient, or employed to stimulate T cells to provide antigen-specific T cells which may, in turn, be administered to a patient. The use of peptide-pulsed dendritic cells to generate antigen-specific T cells and the subsequent use of such antigen-specific T cells to eradicate tumors in a murine model has been demonstrated by Cheever et al. ("Therapy With Cultured T Cells: Principles Revisited," *Immunological Reviews*, 157:177, 1997)

Additionally vectors expressing the disclosed polynucleotides may be introduced into stem cells taken from the patient and clonally propagated *in vitro* for autologous transplant back into the same patient.

In one embodiment, cells of the immune system, such as T cells, may be isolated from the peripheral blood of a patient, using a commercially available cell separation system, such as CellPro Incorporated's (Bothell, WA) CEPRATE™ system (see U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). The separated cells are stimulated with one or more of the immunoreactive polypeptides contained within a delivery vehicle, such as a microsphere, to provide antigen-specific T cells. The population of tumor antigen-specific T cells is then expanded using standard techniques and the cells are administered back to the patient. Polypeptides and fusion proteins of the present invention may also be used to generate binding agents, such as antibodies or fragments thereof, that are capable of detecting metastatic human lung tumors. Binding agents of the present invention may generally be prepared using methods known to those of ordinary skill in the art, including the representative procedures described herein. Binding agents are capable of differentiating between patients with and without lung cancer, using the representative assays described herein. In other words, antibodies or other binding agents raised against a lung tumor protein, or a suitable portion thereof, will generate a signal indicating the presence of primary or metastatic lung cancer in at least about 20% of patients afflicted with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without primary or metastatic lung cancer. Suitable portions of such lung tumor proteins are portions that are able to generate a binding agent that indicates the presence of primary or metastatic lung cancer in substantially all (*i.e.*,

at least about 80%, and preferably at least about 90%) of the patients for which lung cancer would be indicated using the full length protein, and that indicate the absence of lung cancer in substantially all of those samples that would be negative when tested with full length protein. The representative assays described below, such as the two-antibody sandwich
5 assay, may generally be employed for evaluating the ability of a binding agent to detect metastatic human lung tumors.

The ability of a polypeptide prepared as described herein to generate antibodies capable of detecting primary or metastatic human lung tumors may generally be evaluated by raising one or more antibodies against the polypeptide (using, for example, a
10 representative method described herein) and determining the ability of such antibodies to detect such tumors in patients. This determination may be made by assaying biological samples from patients with and without primary or metastatic lung cancer for the presence of a polypeptide that binds to the generated antibodies. Such test assays may be performed, for example, using a representative procedure described below. Polypeptides that generate
15 antibodies capable of detecting at least 20% of primary or metastatic lung tumors by such procedures are considered to be useful in assays for detecting primary or metastatic human lung tumors. Polypeptide specific antibodies may be used alone or in combination to improve sensitivity.

Polypeptides capable of detecting primary or metastatic human lung tumors
20 ~~may be used as markers for diagnosing lung cancer or for monitoring disease progression in~~ patients. In one embodiment, lung cancer in a patient may be diagnosed by evaluating a biological sample obtained from the patient for the level of one or more of the above polypeptides, relative to a predetermined cut-off value. As used herein, suitable "biological samples" include blood, sera, urine and/or lung secretions.

25 The level of one or more of the above polypeptides may be evaluated using any binding agent specific for the polypeptide(s). A "binding agent," in the context of this invention, is any agent (such as a compound or a cell) that binds to a polypeptide as described above. As used herein, "binding" refers to a noncovalent association between two separate molecules (each of which may be free (*i.e.*, in solution) or present on the surface of a cell or a
30 solid support), such that a "complex" is formed. Such a complex may be free or immobilized (either covalently or noncovalently) on a support material. The ability to bind may generally

be evaluated by determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind" in the context of the present invention when the binding constant for complex formation exceeds about 10^3 L/mol. The binding constant may be determined using methods well known to those of ordinary skill in the art.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome with or without a peptide component, an RNA molecule or a peptide. In a preferred embodiment, the binding partner is an antibody, or a fragment thereof. Such antibodies may be polyclonal, or monoclonal. In addition, the antibodies may be single chain, chimeric, CDR-grafted or humanized. Antibodies may be prepared by the methods described herein and by other methods well known to those of skill in the art.

There are a variety of assay formats known to those of ordinary skill in the art for using a binding partner to detect polypeptide markers in a sample. *See, e.g.,* Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In a preferred embodiment, the assay involves the use of binding partner immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a second binding partner that contains a reporter group. Suitable second binding partners include antibodies that bind to the binding partner/polypeptide complex. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding partner after incubation of the binding partner with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding partner is indicative of the reactivity of the sample with the immobilized binding partner.

The solid support may be any material known to those of ordinary skill in the art to which the antigen may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may

be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the antigen and functional groups on the support or may be a linkage by way of a cross-linking agent).
5 Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a
10 well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 μ g, and preferably about 100 ng to about 1 μ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the
15 support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.*, Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

~~In certain embodiments, the assay is a two-antibody sandwich assay.~~ This
20 assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a second antibody
25 (containing a reporter group) capable of binding to a different site on the polypeptide is added. The amount of second antibody that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked.
30 Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is

then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is that period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with lung cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include enzymes (such as horseradish peroxidase), substrates, cofactors, inhibitors, dyes, radionuclides, luminescent groups, fluorescent groups and biotin. The conjugation of antibody to reporter group may be achieved using standard methods known to those of ordinary skill in the art.

The second antibody is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound second antibody is then removed and bound second antibody is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of lung cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal

that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without lung cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for lung cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (i.e., the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for lung cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the antibody is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized antibody as the sample passes through the membrane. A second, labeled antibody then binds to the antibody-polypeptide complex as a solution containing the second antibody flows through the membrane. The detection of bound second antibody may then be performed as described above. In the strip test format, one end of the membrane to which antibody is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second antibody and to the area of immobilized antibody. Concentration of second antibody at the area of immobilized antibody indicates the presence of lung cancer. Typically, the concentration of second antibody at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of antibody immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody

sandwich assay, in the format discussed above. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

5 Of course, numerous other assay protocols exist that are suitable for use with the antigens or antibodies of the present invention. The above descriptions are intended to be exemplary only.

 In another embodiment, the above polypeptides may be used as markers for the progression of lung cancer. In this embodiment, assays as described above for the
10 diagnosis of lung cancer may be performed over time, and the change in the level of reactive polypeptide(s) evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, lung cancer is progressing in those patients in whom the level of polypeptide detected by the binding agent increases over time. In contrast, lung cancer is not progressing when the level of reactive
15 polypeptide either remains constant or decreases with time.

 Antibodies for use in the above methods may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In one such technique, an immunogen comprising the antigenic polypeptide is initially injected into any
20 of a wide variety of mammals (e.g., mice, rats, rabbits, sheep and goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably
25 according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

 Monoclonal antibodies specific for the antigenic polypeptide of interest may
30 be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation

of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Monoclonal antibodies of the present invention may also be used as therapeutic reagents, to diminish or eliminate lung tumors. The antibodies may be used on their own (for instance, to inhibit metastases) or coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ^{90}Y , ^{123}I , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{211}At , and ^{212}Bi . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction

between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker-groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may

be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

Diagnostic reagents of the present invention may also comprise DNA sequences encoding one or more of the above polypeptides, or one or more portions thereof. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify lung tumor-specific cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for a polynucleotide encoding a lung tumor protein of the present invention. The presence of the amplified cDNA is then detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes specific for a polynucleotide encoding a lung tumor protein of the present invention may be used in a hybridization assay to detect the presence of an inventive polypeptide in a biological sample.

As used herein, the term "oligonucleotide primer/probe specific for a polynucleotide" means an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to the polynucleotide in question. Oligonucleotide primers and/or probes which may be usefully employed in the inventive diagnostic methods preferably have at least about 10-40 nucleotides. In a preferred embodiment, the oligonucleotide primers comprise at least about 10 contiguous nucleotides of a polynucleotide having a partial sequence selected from SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181. Preferably, oligonucleotide probes for use in the inventive diagnostic methods comprise at least about 15 contiguous oligonucleotides of a polynucleotide having a partial sequence provided in SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181. Techniques for both PCR based assays and hybridization assays are well known in the art (see, for example, Mullis *et al. Ibid*; Ehrlich, *Ibid*). Primers or probes may thus be used to detect lung tumor-specific sequences in biological samples, including blood, semen, lung tissue and/or lung tumor tissue.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLES

5

Example 1

PREPARATION OF LUNG TUMOR-SPECIFIC cDNA SEQUENCES USING DIFFERENTIAL DISPLAY RT-PCR

This example illustrates the preparation of cDNA molecules encoding lung
10 tumor-specific polypeptides using a differential display screen.

Tissue samples were prepared from breast tumor and normal tissue of a patient
with lung cancer that was confirmed by pathology after removal of samples from the patient.
Normal RNA and tumor RNA was extracted from the samples and mRNA was isolated and
converted into cDNA using a (dT)₁₂AG (SEQ ID NO: 47) anchored 3' primer. Differential
15 display PCR was then executed using a randomly chosen primer (SEQ ID NO: 48).
Amplification conditions were standard buffer containing 1.5 mM MgCl₂, 20 pmol of primer,
500 pmol dNTP and 1 unit of Taq DNA polymerase (Perkin-Elmer, Branchburg, NJ). Forty
cycles of amplification were performed using 94 °C denaturation for 30 seconds, 42 °C
annealing for 1 minute and 72 °C extension for 30 seconds. Bands that were repeatedly
20 observed to be specific to the RNA fingerprint pattern of the tumor were cut out of a silver
stained gel, subcloned into the pGEM-T vector (Promega, Madison, WI) and sequenced. The
isolated 3' sequences are provided in SEQ ID NO: 1-16.

Comparison of these sequences to those in the public databases using the
BLASTN program, revealed no significant homologies to the sequences provided in SEQ ID
25 NO: 1-11. To the best of the inventors' knowledge, none of the isolated DNA sequences
have previously been shown to be expressed at a greater level in human lung tumor tissue
than in normal lung tissue.

Example 2

USE OF PATIENT SERA TO IDENTIFY DNA SEQUENCES ENCODING LUNG
TUMOR ANTIGENS

5 This example illustrates the isolation of cDNA sequences encoding lung tumor antigens by expression screening of lung tumor samples with autologous patient sera.

 A human lung tumor directional cDNA expression library was constructed employing the Lambda ZAP Express expression system (Stratagene, La Jolla, CA). Total RNA for the library was taken from a late SCID mouse passaged human squamous epithelial
10 lung carcinoma and poly A+ RNA was isolated using the Message Maker kit (Gibco BRL, Gaithersburg, MD). The resulting library was screened using *E. coli*-absorbed autologous patient serum, as described in Sambrook et al., (*Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989), with the secondary antibody being goat anti-human IgG-A-M (H + L) conjugated with alkaline phosphatase,
15 developed with NBT/BCIP (Gibco BRL). Positive plaques expressing immunoreactive antigens were purified. Phagemid from the plaques was rescued and the nucleotide sequences of the clones was determined.

 Fifteen clones were isolated, referred to hereinafter as LT86-1 – LT86-15. The isolated cDNA sequences for LT86-1 – LT86-8 and LT86-10 - LT86-15 are provided in
20 SEQ ID NO: 17-24 and 26-31, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 32-39 and 41-46, respectively. The determined cDNA sequence for LT86-9 is provided in SEQ ID NO: 25, with the corresponding predicted amino acid sequences from the 3' and 5' ends being provided in SEQ ID NO: 40 and 65, respectively. These sequences were compared to those in the gene bank as described above.
25 Clones LT86-3, LT86-6 – LT86-9, LT86-11 – LT86-13 and LT86-15 (SEQ ID NO: 19, 22-25, 27-29 and 31, respectively) were found to show some homology to previously identified expressed sequence tags (ESTs), with clones LT86-6, LT86-8, LT86-11, LT86-12 and LT86-15 appearing to be similar or identical to each other. Clone LT86-3 was found to show some homology with a human transcription repressor. Clones LT86-6, 8, 9, 11, 12 and 15 were
30 found to show some homology to a yeast RNA Pol II transcription regulation mediator. Clone LT86-13 was found to show some homology with a *C. elegans* leucine

aminopeptidase. Clone LT86-9 appears to contain two inserts, with the 5' sequence showing homology to the previously identified antisense sequence of interferon alpha-induced P27, and the 3' sequence being similar to LT86-6. Clone LT86-14 (SEQ ID NO: 30) was found to show some homology to the trithorax gene and has an "RGD" cell attachment sequence and a
5 beta-Lactamase A site which functions in hydrolysis of penicillin. Clones LT86-1, LT86-2, LT86-4, LT86-5 and LT86-10 (SEQ ID NOS: 17, 18, 20, 21 and 26, respectively) were found to show homology to previously identified genes. A subsequently determined extended cDNA sequence for LT86-4 is provided in SEQ ID NO: 66, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 67.

10 Subsequent studies led to the isolation of five additional clones, referred to as LT86-20, LT86-21, LT86-22, LT86-26 and LT86-27. The determined 5' cDNA sequences for LT86-20, LT86-22, LT86-26 and LT86-27 are provided in SEQ ID NO: 68 and 70-72, respectively, with the determined 3' cDNA sequences for LT86-21 being provided in SEQ ID NO: 69. The corresponding predicted amino acid sequences for LT86-20, LT86-21, LT86-
15 22, LT86-26 and LT86-27 are provided in SEQ ID NO: 73-77, respectively. LT86-22 and LT86-27 were found to be highly similar to each other. Comparison of these sequences to those in the gene bank as described above, revealed no significant homologies to LT86-22 and LT86-27. LT86-20, LT86-21 and LT86-26 were found to show homology to previously identified genes.

20

Example 3

USE OF MOUSE ANTISERA TO IDENTIFY DNA SEQUENCES ENCODING LUNG
TUMOR ANTIGENS

This example illustrates the isolation of cDNA sequences encoding lung tumor
5 antigens by screening of lung tumor cDNA libraries with mouse anti-tumor sera.

A directional cDNA lung tumor expression library was prepared as described
above in Example 2. Sera was obtained from SCID mice containing late passaged human
squamous cell and adenocarcinoma tumors. These sera were pooled and injected into normal
mice to produce anti-lung tumor serum. Approximately 200,000 PFUs were screened from
10 the unamplified library using this antiserum. Using a goat anti-mouse IgG-A-M (H+L)
alkaline phosphatase second antibody developed with NBT/BCIP (BRL Labs.),
approximately 40 positive plaques were identified. Phage was purified and phagemid excised
for 9 clones with inserts in a pBK-CMV vector for expression in prokaryotic or eukaryotic
cells.

15 The determined cDNA sequences for 7 of the isolated clones (hereinafter
referred to as L86S-3, L86S-12, L86S-16, L86S-25, L86S-36, L86S-40 and L86S-46) are
provided in SEQ ID NO: 49-55, with the corresponding predicted amino acid sequences
being provided in SEQ ID NO: 56-62, respectively. The 5' cDNA sequences for the
remaining 2 clones (hereinafter referred to as L86S-30 and L86S-41) are provided in SEQ ID
20 NO: 63 and 64. L86S-36 and L86S-46 were subsequently determined to represent the same
gene. Comparison of these sequences with those in the public database as described above,
revealed no significant homologies to clones L86S-30, L86S-36 and L86S-46 (SEQ ID NO:
63, 53 and 55, respectively). L86S-16 (SEQ ID NO: 51) was found to show some homology
to an EST previously identified in fetal lung and germ cell tumor. The remaining clones were
25 found to show at least some degree of homology to previously identified human genes.
Subsequently determined extended cDNA sequences for L86S-12, L86S-36 and L86S-46 are
provided in SEQ ID NO: 78-80, respectively, with the corresponding predicted amino acid
sequences being provided in SEQ ID NO: 81-83.

Subsequent studies led to the determination of 5' cDNA sequences for an
30 additional nine clones, referred to as L86S-6, L86S-11, L86S-14, L86S-29, L86S-34, L86S-
39, L86S-47, L86S-49 and L86S-51 (SEQ ID NO: 84-92, respectively). The corresponding

predicted amino acid sequences are provided in SEQ ID NO: 93-101, respectively. L86S-30, L86S-39 and L86S-47 were found to be similar to each other. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to L86S-14. L86S-29 was found to show some homology to a previously identified EST.
5 L86S-6, L86S-11, L86S-34, L86S-39, L86S-47, L86S-49 and L86S-51 were found to show some homology to previously identified genes.

In further studies, a directional cDNA library was constructed using a Stratagene kit with a Lambda Zap Express vector. Total RNA for the library was isolated from two primary squamous lung tumors and poly A+ RNA was isolated using an oligo dT
10 column. Antiserum was developed in normal mice using a pool of sera from three SCID mice implanted with human squamous lung carcinomas. Approximately 700,000 PFUs were screened from the unamplified library with *E. coli* absorbed mouse anti-SCID tumor serum. Positive plaques were identified as described above. Phage was purified and phagemid excised for 180 clones with inserts in a pBK-CMV vector for expression in prokaryotic or
15 eukaryotic cells.

The determined cDNA sequences for 23 of the isolated clones are provided in SEQ ID NO: 126-148. Comparison of these sequences with those in the public database as described above revealed no significant homologies to the sequences of SEQ ID NO: 139 and 143-148. The sequences of SEQ ID NO: 126-138 and 140-142 were found to show
20 homology previously identified human polynucleotide sequences.

Example 4

USE OF MOUSE ANTISERA TO SCREEN LUNG TUMOR LIBRARIES PREPARED
FROM SCID MICE

5 This example illustrates the isolation of cDNA sequences encoding lung tumor antigens by screening of lung tumor cDNA libraries prepared from SCID mice with mouse anti-tumor sera.

A directional cDNA lung tumor expression library was prepared using a Stratagene kit with a Lambda Zap Express vector. Total RNA for the library was taken from
10 a late passaged lung adenocarcinoma grown in SCID mice. Poly A+ RNA was isolated using a Message Maker Kit (Gibco BRL). Sera was obtained from two SCID mice implanted with lung adenocarcinomas. These sera were pooled and injected into normal mice to produce anti-lung tumor serum. Approximately 700,000 PFUs were screened from the unamplified library with *E. coli*-absorbed mouse anti-SCID tumor serum. Positive plaques were identified
15 with a goat anti-mouse IgG-A-M (H+L) alkaline phosphatase second antibody developed with NBT/BCIP (Gibco BRL). Phage was purified and phagemid excised for 100 clones with insert in a pBK-CMV vector for expression in prokaryotic or eukaryotic cells.

The determined 5' cDNA sequences for 33 of the isolated clones are provided in SEQ ID NO: 149-181. The corresponding predicted amino acid sequences for SEQ ID
20 NO: 149, 150, 152-154, 156-158 and 160-181 are provided in SEQ ID NO: 182, 183, 186, 188-193 and 194-215, respectively. The clone of SEQ ID NO: 151 (referred to as SAL-25) was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 184 and 185. The clone of SEQ ID NO:
25 153 (referred to as SAL-50) was found to contain two open reading frames encoding the predicted amino acid sequences of SEQ ID NO: 187 and 216. Similarly, the clone of SEQ ID NO: 155 (referred to as SAL-66) was found to contain two open reading frames encoding the predicted amino acid sequences of SEQ ID NO: 189 and 190. Comparison of the isolated sequences with those in the public database revealed no significant homologies to the sequences of SEQ ID NO: 151, 153 and 154. The sequences of SEQ ID NO: 149, 152, 156,
30 157 and 158 were found to show some homology to previously isolated expressed sequence

tags (ESTs). The sequences of SEQ ID NO: 150, 155 and 159-181 were found to show homology to sequences previously identified in humans.

Example 5

DETERMINATION OF TISSUE SPECIFICITY OF LUNG TUMOR POLYPEPTIDES

Using gene specific primers, mRNA expression levels for representative lung tumor polypeptides were examined in a variety of normal and tumor tissues using RT-PCR.

5 Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent. First strand synthesis was carried out using 2 µg of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β-actin was used as an internal control for each of the
10 tissues examined. 1 µl of 1:30 dilution of cDNA was employed to enable the linear range amplification of the β-actin template and was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β-actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that
15 was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in five different types of tumor tissue (lung squamous tumor from 3 patients, lung adenocarcinoma, prostate tumor colon tumor and breast tumor), and different normal tissues, including lung from four patients, prostate, brain, kidney, liver, ovary, skeletal muscle, skin, small intestine, myocardium, retina and testes.
20 L86S-46 was found to be expressed at high levels in lung squamous tumor, colon tumor and prostate tumor, and was undetectable in the other tissues examined. L86S-5 was found to be expressed in the lung tumor samples and in 2 out of 4 normal lung samples, but not in the other normal or tumor tissues tested. L86S-16 was found to be expressed in all tissues except normal liver and normal stomach. Using real-time PCR, L86S-46 was found to be over-
25 expressed in lung squamous tissue and normal tonsil, with expression being low or undetectable in all other tissues examined.

Example 6

ISOLATION OF DNA SEQUENCES ENCODING LUNG TUMOR ANTIGENS

DNA sequences encoding antigens potentially involved in squamous cell lung
5 tumor formation were isolated as follows.

A lung tumor directional cDNA expression library was constructed employing
the Lambda ZAP Express expression system (Stratagene, La Jolla, CA). Total RNA for the
library was taken from a pool of two human squamous epithelial lung carcinomas and poly
A+ RNA was isolated using oligo-dT cellulose (Gibco BRL, Gaithersburg, MD). Phagemid
10 were rescued at random and the cDNA sequences of isolated clones were determined.

The determined cDNA sequence for the clone SLT-T1 is provided in SEQ ID
NO: 102, with the determined 5' cDNA sequences for the clones SLT-T2, SLT-T3, SLT-T5,
SLT-T7, SLT-T9, SLT-T10, SLT-T11 and SLT-T12 being provided in SEQ ID NO: 103-
110, respectively. The corresponding predicted amino acid sequence for SLT-T1, SLT-T2,
15 SLT-T3, SLT-T10 and SLT-T12 are provided in SEQ ID NO: 111-115, respectively.
Comparison of the sequences for SLT-T2, SLT-T3, SLT-T5, SLT-T7, SLT-T9 and SLT-T11
with those in the public databases as described above, revealed no significant homologies.
The sequences for SLT-T10 and SLT-T12 were found to show some homology to sequences
previously identified in humans.

20 The sequence of SLT-T1 was determined to show some homology to a PAC
clone of unknown protein function. The cDNA sequence of SLT-T1 (SEQ ID NO: 102) was
found to contain a mutator (MUT) domain. Such domains are known to function in removal
of damaged guanine from DNA that can cause A to G transversions (see, for example, el-
Deiry, W.S., 1997 *Curr. Opin. Oncol.* 9:79-87; Okamoto, K. et al. 1996 *Int. J. Cancer*
25 65:437-41; Wu, C. et al. 1995 *Biochem. Biophys. Res. Commun.* 214:1239-45; Porter, D.W.
et al. 1996 *Chem. Res. Toxicol.* 9:1375-81). SLT-T1 may thus be of use in the treatment, by
gene therapy, of lung cancers caused by, or associated with, a disruption in DNA repair.

In further studies, DNA sequences encoding antigens potentially involved in adenocarcinoma lung tumor formation were isolated as follows. A human lung tumor directional cDNA expression library was constructed employing the Lambda ZAP Express expression system (Stratagene, La Jolla, CA). Total RNA for the library was taken from a
5 late SCID mouse passaged human adenocarcinoma and poly A+ RNA was isolated using the Message Maker kit (Gibco BRL, Gaithersburg, MD). Phagemid were rescued at random and the cDNA sequences of isolated clones were determined.

The determined 5' cDNA sequences for five isolated clones (referred to as SALT-T3, SALT-T4, SALT-T7, SALT-T8, and SALT-T9) are provided in SEQ ID NO: 116-
10 120, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 121-125. SALT-T3 was found to show 98% identity to the previously identified human transducin-like enhancer protein TLE2. SALT-T4 appears to be the human homologue of the mouse H beta 58 gene. SALT-T7 was found to have 97% identity to human 3-mercaptopyruvate sulfurtransferase and SALT-T8 was found to show homology to human
15 interferon-inducible protein 1-8U. SALT-T9 shows approximately 90% identity to human mucin MUC 5B.

Example 7

SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems
5 Division 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-
N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence
may be attached to the amino terminus of the peptide to provide a method of conjugation,
binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from
the solid support may be carried out using the following cleavage mixture: trifluoroacetic
10 acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the
peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be
dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to
purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing
0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following
15 lyophilization of the pure fractions, the peptides may be characterized using electrospray or
other types of mass spectrometry and by amino acid analysis.

From the foregoing, it will be appreciated that, although specific embodiments
of the invention have been described herein for the purposes of illustration, various
20 modifications may be made without deviating from the spirit and scope of the invention.

CLAIMS:

1. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:
 - 5 (a) sequences provided in SEQ ID NO: 1-11, 19, 22-25, 27-31, 51, 53, 55, 63, 70, 72, 79, 80, 86, 87, 89, 90, 102-107, 109, 139, 143-149, 151-154 and 156-158;
 - (b) the complements of sequences provided in SEQ ID NO: 1-11, 19, 22-25, 27-31, 51, 53, 55, 63, 70, 72, 79, 80, 86, 87, 89, 90, 102-107, 109, 139, 143-149, 151-154 and 156-158; and
 - 10 (c) variants of the sequences of (a) and (b).
2. An isolated polypeptide comprising an immunogenic portion of a lung tumor protein or a variant thereof, wherein said protein comprises an amino acid sequence encoded by a polynucleotide of claim 1.
- 15 3. The isolated polypeptide of claim 2 wherein the polypeptide comprises a sequence selected from the group of sequences recited in SEQ ID NO: 182, 184-193 and 216.
- 20 4. A polynucleotide comprising a nucleotide sequence encoding the polypeptide of claim 3.
5. An expression vector comprising the polynucleotide of claims 1 or 4.
- 25 6. A host cell transformed with the expression vector of claim 5.
7. The host cell of claim 6 wherein the host cell is selected from the group consisting of *E. coli*, yeast and mammalian cell lines.
- 30 8. A pharmaceutical composition comprising the polypeptide of claim 2 and a physiologically acceptable carrier.

9. A vaccine comprising the polypeptide of claim 2 and an immune response enhancer.

5 10. The vaccine of claim 9 wherein the immune response enhancer is an adjuvant.

11. A vaccine comprising the polynucleotide of claims 1 or 4 and an immune response enhancer.

10 12. The vaccine of claim 11 wherein the immune response enhancer is an adjuvant.

13. A pharmaceutical composition for the treatment of lung cancer
15 comprising a polypeptide and a physiologically acceptable carrier, the polypeptide comprising an immunogenic portion of a lung protein or of a variant thereof, wherein said protein comprises an amino acid sequence encoded by a polynucleotide comprising a sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NO: 12-18, 20, 21, 26, 49, 50, 52, 54, 64,
20 66, 68, 69, 71, 78, 84, 85, 88, 91, 92, 116-120, 126-138, 140-142, 150, 155 and 159-181;

(b) sequences complementary to the sequences of SEQ ID NO: 12-18, 20, 21, 26, 49, 50, 52, 54, 64, 66, 68, 69, 71, 78, 84, 85, 88, 91, 92, 116-120, 126-138, 140-142, 150, 155 and 159-181; and

(c) variants of the sequences of (a) and (b).

25

14. A vaccine for the treatment of lung cancer comprising a polypeptide and an immune response enhancer, said polypeptide comprising an immunogenic portion of a lung protein or of a variant thereof, wherein said protein comprises an amino acid sequence encoded by a polynucleotide comprising a sequence selected from the group consisting of:

30 (a) sequences recited in SEQ ID NO: 12-18, 20, 21, 26, 49, 50, 52, 54, 64, 66, 68, 69, 71, 78, 84, 85, 88, 91, 92, 116-120, 126-138, 140-142, 150, 155 and 159-181;

(b) sequences complementary to the sequences of SEQ ID NO: 12-18, 20, 21, 26, 49, 50, 52, 54, 64, 66, 68, 69, 71, 78, 84, 85, 88, 91, 92, 116-120, 126-138, 140-142, 150, 155 and 159-181; and

(c) variants of the sequences of (a) and (b).

5

15. A vaccine for the treatment of lung cancer comprising a polynucleotide and an immune response enhancer, the polynucleotide comprising a sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NO: 12-18, 20, 21, 26, 49, 50, 52, 54, 64, 66, 68, 69, 71, 78, 84, 85, 88, 91, 92, 116-120, 126-138, 140-142, 150, 155 and 159-181;

(b) sequences complementary to the sequences of SEQ ID NO: 12-18, 20, 21, 26, 49, 50, 52, 54, 64, 66, 68, 69, 71, 78, 84, 85, 88, 91, 92, 116-120, 126-138, 140-142, 150, 155 and 159-181; and

(c) variants of the sequences of (a) and (b).

15

16. A method for inhibiting the development of lung cancer in a patient, comprising administering to the patient an effective amount of the pharmaceutical composition of claims 8 or 13.

20 17. A method for inhibiting the development of lung cancer in a patient, comprising administering to the patient an effective amount of the vaccine of any one of claims 9, 11, 14 or 15.

25 18. A fusion protein comprising at least one polypeptide according to claim 2.

19. A fusion protein comprising at least two polypeptides according to claim 2.

30 20. A fusion protein comprising a polypeptide according to claim 2 and a known lung tumor antigen.

21. A pharmaceutical composition comprising a fusion protein according to any one of claims 18-20 and a physiologically acceptable carrier.

5 22. A vaccine comprising a fusion protein according to any one of claims 18-20 and an immune response enhancer.

23. The vaccine of claim 22 wherein the immune response enhancer is an adjuvant.

10

24. A method for inhibiting the development of lung cancer in a patient, comprising administering to the patient an effective amount of the pharmaceutical composition of claim 21.

15 25. A method for inhibiting the development of lung cancer in a patient, comprising administering to the patient an effective amount of the vaccine of claim 22.

26. A method for inhibiting the development of lung cancer in a patient, comprising administering to the patient a polynucleotide under conditions such that the polynucleotide enters a cell of the patient and is expressed therein, the polynucleotide having a sequence selected from the group consisting of:

20

- (a) a sequence provided in SEQ ID NO: 102;
- (b) sequences complementary to a sequence of SEQ ID NO: 102; and
- (c) variants of the sequence of SEQ ID NO: 102.

25

27. A method for detecting lung cancer in a patient, comprising:

- (a) contacting a biological sample obtained from the patient with a binding agent which is capable of binding to a polypeptide, the polypeptide comprising an immunogenic portion of a lung tumor protein or a variant thereof, wherein said protein comprises an amino acid sequence encoded by a polynucleotide comprising a nucleotide sequence selected from the group consisting of sequences provided in SEQ ID NO: 1-31, 49-

30

55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181, the complements of said sequences and variants thereof; and

(b) detecting in the sample a polypeptide that binds to the binding agent, thereby detecting lung cancer in the patient.

5 28. The method of claim 27 wherein the binding agent is a monoclonal antibody.

 29. The method of claim 28 wherein the binding agent is a polyclonal antibody.

 30. A method for monitoring the progression of lung cancer in a patient,
10 comprising:

 (a) contacting a biological sample obtained from the patient with a binding agent that is capable of binding to a polypeptide, said polypeptide comprising an immunogenic portion of a lung tumor protein or a variant thereof, wherein said protein comprises an amino acid sequence encoded by a polynucleotide comprising a nucleotide
15 sequence selected from the group consisting of sequences recited in SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181, the complements of said sequences and variants thereof;

 (b) determining in the sample an amount of a polypeptide that binds to the binding agent;

20 (c) repeating steps (a) and (b); and

 (d) comparing the amount of polypeptide detected in steps (b) and (c) to monitor the progression of lung cancer in the patient.

 31. A monoclonal antibody that binds to a polypeptide comprising an
25 immunogenic portion of a lung tumor protein or a variant thereof, wherein said protein comprises an amino acid sequence encoded by a polynucleotide comprising a nucleotide sequence selected from the group consisting of:

- 5
- (a) sequences recited in SEQ ID NO: 1-11, 19, 22-25, 27-31, 51, 53, 55, 63, 70, 72, 79, 80, 86, 87, 89, 90, 102-107, 109, 139, 143-149, 151-154 and 156-158;
 - (b) the complements of nucleotide sequences recited in SEQ ID NO: 1-11, 19, 22-25, 27-31, 51, 53, 55, 63, 70, 72, 79, 80, 86, 87, 89, 90, 102-107, 109, 139, 143-149, 151-154 and 156-158; and
 - (c) variants of the sequences of (a) and (b).

10 32. A method for inhibiting the development of lung cancer in a patient, comprising administering to the patient a therapeutically effective amount of a monoclonal antibody according to claim 31.

33. The method of claim 32 wherein the monoclonal antibody is conjugated to a therapeutic agent.

- 15 34. A method for detecting lung cancer in a patient comprising:
- (a) obtaining a biological sample from the patient;
 - (b) contacting the sample with at least two oligonucleotide primers in a polymerase chain reaction, wherein at least one of the oligonucleotides is specific for a polynucleotide encoding a polypeptide comprising an immunogenic portion of a lung tumor protein or a variant thereof, said protein comprising an amino acid sequence encoded by a polynucleotide comprising a nucleotide sequence selected from the group consisting of
- 20 sequences recited in SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181, the complements of said sequences and variants thereof; and
- (c) detecting in the sample a DNA sequence that amplifies in the presence of the oligonucleotide primers, thereby detecting lung cancer.

25 35. The method of claim 34, wherein at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of a polynucleotide comprising a sequence selected from SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181.

36. A diagnostic kit comprising:
- (a) one or more monoclonal antibodies according to claim 31; and
 - (b) a detection reagent.
37. The kit of claim 36 wherein the monoclonal antibody is immobilized
5 on a solid support.
38. The kit of claim 37 wherein the solid support comprises nitrocellulose, latex or a plastic material.
39. The kit of claim 36 wherein the detection reagent comprises a reporter group conjugated to a binding agent.
- 10 40. The kit of claim 39 wherein the binding agent is selected from the group consisting of anti-immunoglobulins, Protein G, Protein A and lectins.
41. The kit of claim 39 wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.
- 15 42. A diagnostic kit comprising at least two oligonucleotide primers, at least one of the oligonucleotide primers being specific for a polynucleotide encoding a polypeptide comprising an immunogenic portion of a lung tumor protein or a variant thereof, said protein comprising an amino acid sequence encoded by a polynucleotide comprising a nucleotide sequence selected from the group consisting of sequences recited in SEQ ID NO:
20 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181, the complements of said sequences and variants thereof.
43. The diagnostic kit of claim 42 wherein at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of a polynucleotide having a nucleotide sequence selected from the group consisting of sequences

provided in SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181, the complements of said sequences and variants thereof.

44. A method for detecting lung cancer in a patient, comprising:

(a) obtaining a biological sample from the patient;

5 (b) contacting the biological sample with an oligonucleotide probe specific for a polynucleotide encoding a polypeptide comprising an immunogenic portion of a lung tumor protein or a variant thereof, said protein comprising an amino acid sequence encoded by a polynucleotide comprising a nucleotide sequence selected from the group consisting of sequences recited in SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181, the complements of said nucleotide sequences and variants thereof; and

10 (c) detecting in the sample a DNA sequence that hybridizes to the oligonucleotide probe, thereby detecting lung cancer in the patient.

45. The method of claim 44 wherein the oligonucleotide probe comprises at least about 15 contiguous nucleotides of a polynucleotide having a nucleotide sequence selected from the group consisting of sequences recited in SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181, the complements of said nucleotide sequences and variants thereof.

46. A diagnostic kit comprising an oligonucleotide probe specific for a polynucleotide encoding a polypeptide comprising an immunogenic portion of a lung tumor protein or a variant thereof, said protein comprising an amino acid sequence encoded by a polynucleotide comprising a nucleotide sequence selected from the group consisting of sequences recited in SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181, the complements of said sequences and variants thereof.

47. The diagnostic kit of claim 46, wherein the oligonucleotide probe comprises at least about 15 contiguous nucleotides of a polynucleotide having a nucleotide sequence selected from the group consisting of sequences recited in SEQ ID NO: 1-31, 49-55,

63, 64, 66, 68-72, 78-80, 84-92 and 102-110, the complements of said sequences and variants thereof.

- 5 48. A method for treating lung cancer in a patient, comprising the steps of:
 (a) obtaining peripheral blood cells from the patient;
 (b) incubating the cells in the presence of at least one polypeptide of claim
 2, such that T cells proliferate; and
 (c) administering the proliferated T cells to the patient.
- 10 49. A method for treating lung cancer in a patient, comprising the steps of:
 (a) obtaining peripheral blood cells from the patient;
 (b) incubating the cells in the presence of at least one polynucleotide of
 claim 1, such that T cells proliferate; and
 (c) administering to the patient the proliferated T cells.
- 15 50. The method of any one of claims 48 and 49 wherein the step of
 incubating the T cells is repeated one or more times.
- 20 51. The method of any one of claims 48 and 49 wherein step (a) further
 comprises separating T cells from the peripheral blood cells, and the cells incubated in step
 (b) are the T cells.
- 25 52. The method of any one of claims 48 and 49 wherein step (a) further
 comprises separating CD4+ cells or CD8+ cells from the peripheral blood cells, and the cells
 proliferated in step (b) are CD4+ or CD8+ T cells.
53. The method of any one of claims 48 and 49 wherein step (b) further
 comprises cloning one or more T cells that proliferated in the presence of the polypeptide.
- 30 54. A composition for the treatment of lung cancer in a patient, comprising
 T cells proliferated in the presence of a polypeptide of claim 2, in combination with a

pharmaceutically acceptable carrier.

55. A composition for the treatment of lung cancer in a patient, comprising
T cells proliferated in the presence of a polynucleotide of claim 1, in combination with a
5 pharmaceutically acceptable carrier.

56. A method for treating lung cancer in a patient, comprising the steps of:
(a) incubating antigen presenting cells in the presence of at least one
polypeptide of claim 2; and
10 (b) administering to the patient the incubated antigen presenting cells.

57. A method for treating lung cancer in a patient, comprising the steps of:
(a) incubating antigen presenting cells in the presence of at least one
polynucleotide of claim 1; and
15 (b) administering to the patient the incubated antigen presenting cells.

58. The method of claims 54 or 55 wherein the antigen presenting cells are
selected from the group consisting of dendritic cells and macrophage cells.

20 59. A composition for the treatment of lung cancer in a patient, comprising
antigen presenting cells incubated in the presence of a polypeptide of claim 2, in combination
with a pharmaceutically acceptable carrier.

25 60. A composition for the treatment of lung cancer in a patient, comprising
antigen presenting cells incubated in the presence of a polynucleotide of claim 1, in
combination with a pharmaceutically acceptable carrier.

SEQUENCE LISTING

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543

<210> 12

<211> 329

<212> DNA

<213> Homo sapiens

<400> 12

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ggcaagacca taggtgggt gctgggaatc ctggggccg gctggcacc actcctgggt 180
ctcaagggag agaccactt gttcagatgc atrggcctca ggcggttcaa ggcrgtctta 240
gagccacaga gtcaaataaa aatcaatttt gagagaccac ageacctget gctttgatcg 300
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329

<210> 13

<211> 314

<212> DNA

<213> Homo sapiens

<400> 13

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catgaagggg gcaccgtgga gaagacagt gcccctacag aatgttcata ggttcccnac 240
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314

<210> 14

<211> 691

<212> DNA

<213> Homo sapiens

<400> 14

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nggtycaacc wttttgggaa mamcycccc c 691
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<210> 15

<211> 355

<212> DNA

<213> Homo sapiens

<400> 15

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cagttcgagc ctctnaagag cgtctaagcg atggggatat atatttactg gagaatgggc 240
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<210> 16

<211> 522

<212> DNA

<213> Homo sapiens

<400> 16

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tgactgcatt gccgctgtat naaagcatgt ggtcttacag tgttnggacn gctnatnaat 420
ttnatcctnc tntgtaatac ttctatgtg acatttctct tccccctgga aacactgcan 480
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<210> 17

<211> 317

<212> DNA

<213> Homo sapiens

<400> 17

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gagaatggca aaattagttg ccttcgtcga gagtgcctct ctgatgaatg tgggtgctgg 180
gtgtttatgg caagtcactt tgacagacat tatttgggca aatgttgcct gaccactgt 240
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ttcaactaac cagaagacaa gtaactgtat gagttaatta aagacatgaa ctaaaaaaaaa 300
aaaaaaaaaa actcgag 317

<210> 18

<211> 392

<212> DNA

<213> Homo sapiens

<400> 18

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agaagccccct gaccccttat ttccgcttct tcatggagaa gcggggccaag tatgcgaaac 180
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gagcgaaaacc tggcccgatt caggaggatg cccccccacc ttatccagaa tgccaagaat 360
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<210> 19

<211> 2624

<212> DNA

<213> Homo sapiens

<400> 19

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tcttgggctg cccactgccc gatcctaata actattatca ccgacgtaac gagatgacca 180
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<210> 20

<211> 488

<212> DNA

<213> Homo sapiens

<400> 20

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gctccgcagg gtgaggtggc tttagccccg ggttgccccg ccagcacgac cgaggaggtg 120
gctggacagc tggaggatga acggagaagc cgactgcccc acagacctgg aaatggccgc 180
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gaacaacctt ccatccaatg acagctccca gttcaaaacc acccaaacac acatggaccg 300
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<210> 21

<211> 391

<212> DNA

<213> Homo sapiens

<400> 21

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<210> 22

<211> 1320

<212> DNA

<213> Homo sapiens

<400> 22

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gtggtcaaaa tgcagaggct aacattagaa cacttgaatc agatggttgg aatcgagtac 180
atccttttgc atgctcaaga gccattctt ttcattctt ggaagcaaca gcggcagtc 240
cctgcccagg ttatcccact agctgattac tatatcatt ctggagtgat ctatcaggca 300
ccagacttgg gatcagttat aaactctaga gtgcttactg cagtgcattg tattcagtca 360

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gcttttgatg aagctatgtc atactgtcga tatcatcctt ccaaagggtg ttggtggcac 420
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<210> 23

<211> 633

<212> DNA

<213> Homo sapiens

<400> 23

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gaaagatgta aattagcaga aaaaaactc gag 633

<210> 24

<211> 1328

<212> DNA

<213> Homo sapiens

<400> 24

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1328

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<210> 25

<211> 1758

<212> DNA

<213> Homo sapiens

<400> 25

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aaaaaaaaaa aactcgag
1758

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<210> 26

<211> 493

<212> DNA

<213> Homo sapiens

<400> 26

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agctttccga gcggacgagc cggccgtgcc gggcatcccc agcctcgcta ccctcgagc 120

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acacgtcgag ccccgcacag gcaagggtcc ggaacttagc ccaaagcacg tttcccctgg 180
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ccgtcttcgt catgggtggg cccccccgccc cggggcaaga cctactttctc cagaaaagct 480
tactcgctgc ctc
493

<210> 27

<211> 1331

<212> DNA

<213> Homo sapiens

<400> 27

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gagacttcag tgagtactgg acaaaagaga agcctggaag actcctcatg ctagtatatca 780
tacctcagta ctgtggctct tgagctttga agtactttat tgtaaccttc ttatttctat 840
ggaatgcgct tattttttga aaggatatta ggccggatgt ggtggctcac gcctgtaac 900
ccagcacttt gggaggccat ggcggtgga tcacttgagg tcagaagttc aagaccagcc 960
tgaccaatat ggtgaaaccc cgtctctact aaaaatacaa aaattagccg ggcgtgggtg 1020
cgggcgcccc tagtcccagc tactcgggag gctgagacag gagacttgct tgaaccggg 1080
aggtggagggt tgccctgagc tgattatcat gctgttgac tccagcttgg gcgacagagc 1140
gagactttgt ctcaaaaaaa gaagaaaaga tattattccc atcatgattt cttgtgaata 1200
tttgttatat gtcttctgta accttctctc tcccggactt gagcaacctc cacactcaca 1260
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aaaaactcga g
1331

<210> 28

<211> 1333

<212> DNA

<213> Homo sapiens

<400> 28

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acagaacatg taataatgaa gtggtcaaaa tgcagaggct aacattagaa cacttgaatc 180
agatgggtcgg aatcgagtac atccttttgc atgctcaaga gccattctt ttcattcatc 240
ggaagcaaca gcggcagtc cctgcccagg ttatcccact agctgattac tatatcattg 300
ctggagtgat ctatcaggca ccagacttgg gatcagttat aaactctaga gtgcttactg 360
cagtgcagtg tatttcagtc gcttttgatg aagctatgtc atactgtcga tatcatcctt 420
ccaaagggta ttggtggcac ttcaaagatc atgaagagca agataaagtc agacctaaag 480
ccaaaggaa agaagaacca agctctattt ttcagagaca acgtgtggat gctttacttt 540
tagacctcag acaaaaattt ccacccaaat ttgtgcagct aaagcctgga gaaaagcctg 600
ttccagtgga tcaaacaaag aaagaggcag aacctatacc agaaactgta aaacctgagg 660

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agaaggagac cacaaagaat gtacaacaga cagtgagtgc taaaggcccc cctgaaaaaac 720
ggatgagact tcagttagta ctggacaaaa gagaagcctg gaagactcct catgctagtt 780
atcatacctc agtactgtgg ctcttgagct ttgaagtact ttattgtaac cttcttattt 840
gtatggaatg cgcttatatt ttgaaaggat attaggccgg atgtggtggc tcacgcctgt 900
aatcccagca ctttggggagg ccattggcggg tggatcactt gaggtcagaa gttcaagacc 960
agcctgacca atatggtgaa accccgtctc tactaaaaat acaaaaatta gccgggcgtg 1020
gtggcgggcg cccatagtcc cagctactcg ggaggctgag acaggagact tgcttgaacc 1080
cgggaggtgg aggttgccct gagctgatta tcatgctgtt gcactccagc ttgggcgaca 1140
gagcgagact ttgtctcaaa aaagaagaaa agatattatt cccatcatga tttcttgtga 1200
atatttgtga tatgtcttct gtaacctttc ctctcccgga cttgagcaac ctacacactc 1260
acatgtttac tggtagatat gtttaaaagc aaaataaagg tatttgtata aaaaaaaaaa 1320
aaaaaaaaactc gag

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1333

<210> 29

<211> 813

<212> DNA

<213> Homo sapiens

<400> 29

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ctgagctgca cttcagcgaa ttcacctcgg ctgtggctga catgaagaac tccgtggcgg 60
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actggccccg ggctgggtgc cacctggaca tcgctgctcc agtgcattgt ggcgagcgag 180
ccacaggctt tgggggtggc ctccctactg ctcttttttg ccgtgcctcc gaggaccctg 240
tgctgaacct ggtatccccg ctggactgtg aggtggatgc ccaggaaagg gacaacatgg 300
ggcgtgactc caagagacgg aggcctcgtg gagggctact tcccagctgg tgacacaggg 360
ttccttacct cattttgac tgactgattt taagcaattg aaagattaac taactcttaa 420
gatgagtttg gcttctcctt ctgtgcccag tgggtacagg agtgagccat tcttctctta 480
gaagcagctt aggggcttgg tgggggtctg agaaaattgt cacagacccc ataggctctcc 540
atctgtaaag cctgtccctt gtccctccacc ctggtcttta gagccacctc aggtcacctc 600
ctgtagttag tgtacttctt gacccaggcc cttgctcaag ctggggctcc ctgggggtgtc 660
taaccagccc tgggttagatg tgactggctg ttagggaccc cattctgtga agcaggagac 720
cctcacagct cccaccaacc cccagttcac ttgaagttga attaaatatg gccacaacat 780
aaaaaaaaaa aaaaaaaaaa aaaaaaactc gag

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813

<210> 30

<211> 1316

<212> DNA

<213> Homo sapiens

<400> 30

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cagtccaatc atagaaaaga tggaaaaaag gacatgtgcc ctgtgccctg aagggcacga 120
gtggagtcaa atatactttt caccatcagg aaatatagtt gctcatgaaa actgttttgt 180
gtattcatca ggactggtgg agtgtgagac tcttgatcta cgtaatacaa ttgaaaactt 240
tgatgtcaaa tctgtaaaga aagagatctg gagaggaaga agattgaaat gctcattctg 300
taacaaagga ggcgccaccg tgggggtgtg tttatggttc tgtaagaaga gttaccacta 360
tgtctgtgcc aaaaaggacc aagcaattct tcaagtgtat ggaaaccatg gaacttacia 420
attattttgc ccagaacatt ctccagaaca agaagaggcc actgaaagtg ctgatgacct 480
aagcatgaag aagaagagag gaaaaaacaa acgctctca tcaggccctc ctgcacagcc 540
aaaaacgatg aaatgtagta acgccaagg acatatgaca gaagagcctc atggtcacac 600
agatgcagct gtcaaatctc cttttcttaa gaaatgccag gaagcaggac ttcttactga 660
actatttgaa cacatactag aaaatatgga ttacgttcat ggaagacttg tggatgagac 720
tgctctagag tcggactatg aagggtatga gaccttactg tttgactgtg gattattcaa 780
agacacacta agaaaattcc aagaagtaat caagagtaaa gcttgtgaat gggaagaaa 840
gcaaaggcag atgaagcagc agcttgaggc acctgcagac ttacaacaaa gcttgtgtctc 900

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atttcaagaa aat'ggggacc tggactgctc aagttctaca tcaggatcct tgctacctcc 960
tgaggaccac cagtaaaagc tgttctcag gaaaactgga tggggcctcc atgttctcca 1020
aggatcgagg aagtcttctt gcctacctg cccacccag tcaagggcag caacaccaga 1080
gctttgctca gccttaaag gaactcttaga gcttctctt gcttctgcta ctctacaga 1140
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actgtgcatt gcacactgtt accatgggtt tatgtctact atcatatcac attgccaata 1260
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<210> 31

<211> 1355

<212> DNA

<213> Homo sapiens

<400> 31

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ctattttgaa cagtggtagt gtcctggatt acttttcaga aagaagtaat cctttttatg 120
acagaacatg taataatgaa gtggtcaaaa tgcagaggct aacattagaa cacttgaatc 180
agatgggttg aatcgagtag atccttttgc atgtctcaaga gccattctt ttcattatc 240
ggaagcaaca gcgcagatcc cctgcccagg ttatcccact agctgattac tatatcattg 300
ctggagtgat ctatcaggca ccagacttgg gatcagttat aaactctaga gtgcttactg 360
cagtgcattg tattcagtca gcttttgatg aagctatgtc atactgtcga tatcatcctt 420
ccaaagggtg ttggtggcac ttcaaagatc atgaagagca agataaagtc agacctaaag 480
ccaaaaggaa agaagaacca agctctatct ttcagagaca acgtgtggat gctttacttt 540
tagacctcag acaaaaattt ccacccaaat ttgtgcagct aaagcctgga gaaaagcctg 600
ttccagtggg tcaaaacaaag aaagaggcag aacctatacc agaaactgta aaacctgagg 660
agaaggagac cacaaagaat gtacaacaga cagtgagtgc taaaggcccc cctgaaaaaac 720
ggatgagact tcagttagta ctggacaaaa gagaagcctg gaagactcct catgctagtt 780
atcatacctc agtactgtgg ctcttgagct ttgaaagtact ttattgtaac cttcttattt 840
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aatcccagca ctttgggagg ccatggcggg tggatcactt gaggtcagaa gttcaagacc 960
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cgggaggttg aggttgccct gagctgatta tcatgctgtt gcactccagc ttgggcgaca 1140
gaacgagact ttgtctcaaa aaaaagaagaa aagatattat tcccatcatg atttcttctg 1200
aatatttctt atatgtcttc tggtaacctt tctctcccg gacttgaagc aacctcacac 1260
actcacatgt ttactggtag atatgtttta aaagcaaaat aaaggatatt gtttttccaa 1320
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa tcgag 1355

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<210> 32

<211> 80

<212> PRT

<213> Homo sapiens

<400> 32

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Val Ser Arg Ile Arg Gly Gly Ala Lys Lys Arg Lys Lys Lys Ser Tyr
  1                               5                               10                               15
Thr Thr Pro Lys Lys Asp Lys His Gln Arg Lys Lys Val Gln Pro Ala
                20                               25                               30
Val Leu Lys Tyr Tyr Lys Val Asp Glu Asn Gly Lys Ile Ser Cys Leu
                35                               40                               45
Arg Arg Glu Cys Pro Ser Asp Glu Cys Gly Ala Gly Val Phe Met Ala
                50                               55                               60

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Ser His Phe Asp Arg His Tyr Cys Gly Lys Cys Cys Leu Thr His Cys
 65 70 75 80

<210> 33
 <211> 130
 <212> PRT
 <213> Homo sapiens

<400> 33
 Glu Ile Ser Asn Glu Val Arg Lys Phe Arg Thr Leu Thr Glu Leu Ile
 1 5 10 15
 Leu Asp Ala Gln Glu His Val Lys Asn Pro Tyr Lys Gly Lys Lys Leu
 20 25 30
 Lys Lys His Pro Asp Phe Pro Lys Lys Pro Leu Thr Pro Tyr Phe Arg
 35 40 45
 Phe Phe Met Glu Lys Arg Ala Lys Tyr Ala Lys Leu His Pro Gln Met
 50 55 60
 Ser Asn Leu Asp Leu Thr Lys Ile Leu Ser Lys Lys Tyr Lys Glu Leu
 65 70 75 80
 Pro Glu Lys Lys Lys Met Lys Tyr Val Pro Asp Phe Gln Arg Arg Glu
 85 90 95
 Thr Gly Val Arg Ala Lys Pro Gly Pro Ile Gln Gly Gly Ser Pro Pro
 100 105 110
 Pro Tyr Pro Glu Cys Gln Glu Ser Asp Ile Pro Glu Lys Pro Gln Asp
 115 120 125
 Pro Pro
 130

<210> 34
 <211> 506
 <212> PRT
 <213> Homo sapiens

<400> 34
 Asn Ser Glu Lys Glu Ile Pro Val Leu Asn Glu Leu Pro Val Pro Met
 1 5 10 15
 Val Ala Arg Tyr Ile Arg Ile Asn Pro Gln Ser Trp Phe Asp Asn Gly
 20 25 30
 Ser Ile Cys Met Arg Met Glu Ile Leu Gly Cys Pro Leu Pro Asp Pro

35	40	45
Asn Asn Tyr Tyr His Arg Arg Asn Glu Met Thr Thr Thr Asp Asp Leu		
50	55	60
Asp Phe Lys His His Asn Tyr Lys Glu Met Arg Gln Leu Met Lys Val		
65	70	75
		80
Val Asn Glu Met Cys Pro Asn Ile Thr Arg Ile Tyr Asn Ile Gly Lys		
	85	90
		95
Ser His Gln Gly Leu Lys Leu Tyr Ala Val Glu Ile Ser Asp His Pro		
100	105	110
Gly Glu His Glu Val Gly Glu Pro Glu Phe His Tyr Ile Ala Gly Ala		
115	120	125
His Gly Asn Glu Val Leu Gly Arg Glu Leu Leu Leu Leu Leu His		
130	135	140
Phe Leu Cys Gln Glu Tyr Ser Ala Gln Asn Ala Arg Ile Val Arg Leu		
145	150	155
		160
Val Glu Glu Thr Arg Ile His Ile Leu Pro Ser Leu Asn Pro Asp Gly		
	165	170
		175
Tyr Glu Lys Ala Tyr Glu Gly Gly Ser Glu Leu Gly Gly Trp Ser Leu		
180	185	190
Gly Arg Trp Thr His Asp Gly Ile Asp Ile Asn Asn Asn Phe Pro Asp		
195	200	205
Leu Asn Ser Leu Leu Trp Glu Ala Glu Asp Gln Gln Asn Ala Pro Arg		
210	215	220
Lys Val Pro Asn His Tyr Ile Ala Ile Pro Glu Trp Phe Leu Ser Glu		
225	230	235
		240
Asn Ala Thr Val Ala Thr Glu Thr Arg Ala Val Ile Ala Trp Met Glu		
	245	250
		255
Lys Ile Pro Phe Val Leu Gly Gly Asn Leu Gln Gly Gly Glu Leu Val		
260	265	270
Val Ala Tyr Pro Tyr Asp Met Val Arg Ser Leu Trp Lys Thr Gln Glu		
275	280	285
His Thr Pro Thr Pro Asp Asp His Val Phe Arg Trp Leu Ala Tyr Ser		
290	295	300
Tyr Ala Ser Thr His Arg Leu Met Thr Asp Ala Arg Arg Arg Val Cys		
305	310	315
		320
His Thr Glu Asp Phe Gln Lys Glu Glu Gly Thr Val Asn Gly Ala Ser		
	325	330
		335

Trp His Thr Val Ala Gly Ser Leu Asn Asp Phe Ser Tyr Leu His Thr
 340 345 350
 Asn Cys Phe Glu Leu Ser Ile Tyr Val Gly Cys Asp Lys Tyr Pro His
 355 360 365
 Glu Ser Glu Leu Pro Glu Glu Trp Glu Asn Asn Arg Glu Ser Leu Ile
 370 375 380
 Val Phe Met Glu Gln Val His Arg Gly Ile Lys Gly Ile Val Arg Asp
 385 390 395 400
 Leu Gln Gly Lys Gly Ile Ser Asn Ala Val Ile Ser Val Glu Gly Val
 405 410 415
 Asn His Asp Ile Arg Thr Ala Ser Asp Gly Asp Tyr Trp Arg Leu Leu
 420 425 430
 Asn Pro Gly Glu Tyr Val Val Thr Ala Lys Ala Glu Gly Phe Ile Thr
 435 440 445
 Ser Thr Lys Asn Cys Met Val Gly Tyr Asp Met Gly Ala Thr Arg Cys
 450 455 460
 Asp Phe Thr Leu Thr Lys Thr Asn Leu Ala Arg Ile Arg Glu Ile Met
 465 470 475 480
 Glu Thr Phe Gly Lys Gln Pro Val Ser Leu Pro Ser Arg Arg Leu Lys
 485 490 495
 Leu Arg Gly Arg Lys Arg Arg Gln Arg Gly
 500 505

<210> 35
 <211> 96
 <212> PRT
 <213> Homo sapiens

<400> 35
 Met Asn Gly Glu Ala Asp Cys Pro Thr Asp Leu Glu Met Ala Ala Pro
 1 5 10 15
 Arg Gly Gln Asp Arg Trp Ser Gln Glu Asp Met Leu Thr Leu Leu Glu
 20 25 30
 Cys Met Lys Asn Asn Leu Pro Ser Asn Asp Ser Ser Gln Phe Lys Thr
 35 40 45
 Thr Gln Thr His Met Asp Arg Glu Lys Val Ala Leu Lys Asp Phe Ser
 50 55 60
 Gly Asp Met Cys Lys Leu Lys Trp Val Glu Ile Ser Asn Glu Val Arg
 65 70 75 80

Lys Phe Arg Thr Leu Thr Glu Leu Ile Leu Asp Thr Gln Glu His Val
 85 90 95

<210> 36
 <211> 129
 <212> PRT
 <213> Homo sapiens

<400> 36
 Gly Ile Val Val Phe Ser Leu Gly Ser Met Val Ser Glu Ile Pro Glu
 1 5 10 15

Lys Lys Ala Val Ala Ile Ala Asp Ala Leu Gly Lys Ile Pro Gln Thr
 20 25 30

Val Leu Trp Arg Tyr Thr Gly Thr Arg Pro Ser Asn Leu Ala Asn Asn
 35 40 45

Thr Ile Leu Val Gln Trp Leu Pro Gln Asn Asp Leu Leu Gly His Pro
 50 55 60

Met Thr Arg Ala Phe Ile Thr His Ala Ser Ser His Gly Val Asn Glu
 65 70 75 80

Ser Ile Cys Asn Gly Val Pro Met Val Met Ile Pro Leu Phe Gly Asp
 85 90 95

Gln Met Asp Asn Ala Lys Arg Arg Glu Thr Lys Gly Ala Gly Val Thr
 100 105 110

Leu Asn Val Leu Glu Met Thr Ser Glu Asp Leu Glu Asp Ala Leu Lys
 115 120 125

Ser

<210> 37
 <211> 238
 <212> PRT
 <213> Homo sapiens

<400> 37
 Asn Leu Leu Gly Ile Ser Trp Val Asp Ser Ser Trp Ile Pro Ile Leu
 1 5 10 15

Asn Ser Gly Ser Val Leu Asp Tyr Phe Ser Glu Arg Ser Asn Pro Phe
 20 25 30

Tyr Asp Arg Thr Cys Asn Asn Glu Val Val Lys Met Gln Arg Leu Thr
 35 40 45

Leu Glu His Leu Asn Gln Met Val Gly Ile Glu Tyr Ile Leu Leu His
 50 55 60

Ala Gln Glu Pro Ile Leu Phe Ile Ile Arg Lys Gln Gln Arg Gln Ser
 65 70 75 80
 Pro Ala Gln Val Ile Pro Leu Ala Asp Tyr Tyr Ile Ile Ala Gly Val
 85 90 95
 Ile Tyr Gln Ala Pro Asp Leu Gly Ser Val Ile Asn Ser Arg Val Leu
 100 105 110
 Thr Ala Val His Gly Ile Gln Ser Ala Phe Asp Glu Ala Met Ser Tyr
 115 120 125
 Cys Arg Tyr His Pro Ser Lys Gly Tyr Trp Trp His Phe Lys Asp His
 130 135 140
 Glu Glu Gln Asp Lys Val Arg Pro Lys Ala Lys Arg Lys Glu Glu Pro
 145 150 155 160
 Ser Ser Ile Phe Gln Arg Gln Arg Val Asp Ala Leu Leu Leu Asp Leu
 165 170 175
 Arg Gln Lys Phe Pro Pro Lys Phe Val Gln Leu Lys Pro Gly Glu Lys
 180 185 190
 Pro Val Pro Val Asp Gln Thr Lys Lys Glu Ala Glu Pro Ile Pro Glu
 195 200 205
 Thr Val Lys Pro Glu Glu Lys Glu Thr Thr Lys Asn Val Gln Gln Thr
 210 215 220
 Val Ser Ala Lys Gly Pro Pro Glu Lys Arg Met Arg Leu Gln
 225 230 235
 <210> 38
 <211> 202
 <212> PRT
 <213> Homo sapiens
 <400> 38
 Lys Gly Ser Glu Gly Glu Asn Pro Leu Thr Val Pro Gly Arg Glu Lys
 1 5 10 15
 Glu Gly Met Leu Met Gly Val Lys Pro Gly Glu Asp Ala Ser Gly Pro
 20 25 30
 Ala Glu Asp Leu Val Arg Arg Ser Glu Lys Asp Thr Ala Ala Val Val
 35 40 45
 Ser Arg Gln Gly Ser Ser Leu Asn Leu Phe Glu Asp Val Gln Ile Thr
 50 55 60
 Glu Pro Glu Ala Glu Pro Glu Ser Lys Ser Glu Pro Arg Pro Pro Ile
 65 70 75 80

Ser Ser Pro Arg Ala Pro Gln Thr Arg Ala Val Lys Pro Arg Leu His
 85 90 95
 Pro Val Lys Pro Met Asn Ala Thr Ala Thr Lys Val Ala Asn Cys Ser
 100 105 110
 Leu Gly Thr Ala Thr Ile Ile Gly Glu Asn Leu Asn Asn Glu Val Met
 115 120 125
 Met Lys Lys Tyr Ser Pro Ser Asp Pro Ala Phe Ala Tyr Ala Gln Leu
 130 135 140
 Thr His Asp Glu Leu Ile Gln Leu Val Leu Lys Gln Lys Glu Thr Ile
 145 150 155 160
 Ser Lys Lys Glu Phe Gln Val Arg Glu Leu Glu Asp Tyr Ile Asp Asn
 165 170 175
 Leu Leu Val Arg Val Met Glu Glu Thr Pro Asn Ile Leu Arg Ile Pro
 180 185 190
 Thr Gln Val Gly Lys Lys Ala Gly Lys Met
 195 200

<210> 39

<211> 243

<212> PRT

<213> Homo sapiens

<400> 39

Val Asn Ala Leu Gly Ile Met Ala Ala Val Asp Ile Arg Asp Asn Leu
 1 5 10 15
 Leu Gly Ile Ser Trp Val Asp Ser Ser Trp Ile Pro Ile Leu Asn Ser
 20 25 30
 Gly Ser Val Leu Asp Tyr Phe Ser Glu Arg Ser Asn Pro Phe Tyr Asp
 35 40 45
 Arg Thr Cys Asn Asn Glu Val Val Lys Met Gln Arg Leu Thr Leu Glu
 50 55 60
 His Leu Asn Gln Met Val Gly Ile Glu Tyr Ile Leu Leu His Ala Gln
 65 70 75 80
 Glu Pro Ile Leu Phe Ile Ile Arg Lys Gln Gln Arg Gln Ser Pro Ala
 85 90 95
 Gln Val Ile Pro Leu Ala Asp Tyr Tyr Ile Ile Ala Gly Val Ile Tyr
 100 105 110
 Gln Ala Pro Asp Leu Gly Ser Val Ile Asn Ser Arg Val Leu Thr Ala
 115 120 125

Val His Gly Ile Gln Ser Ala Phe Asp Glu Ala Met Ser Tyr Cys Arg
 130 135 140
 Tyr His Pro Ser Lys Gly Tyr Trp Trp His Phe Lys Asp His Glu Glu
 145 150 155 160
 Gln Asp Lys Val Arg Pro Lys Ala Lys Arg Lys Glu Glu Pro Ser Ser
 165 170 175
 Ile Phe Gln Arg Gln Arg Val Asp Ala Leu Leu Leu Asp Leu Arg Gln
 180 185 190
 Lys Ile Ser Thr Gln Ile Cys Ala Val Asp Gln Thr Lys Lys Glu Ala
 195 200 205
 Glu Pro Ile Pro Glu Thr Val Lys Pro Glu Glu Lys Glu Thr Thr Lys
 210 215 220
 Asn Val Gln Gln Thr Val Ser Ala Lys Gly Pro Pro Glu Lys Arg Met
 225 230 235 240
 Arg Leu Gln

 <210> 40
 <211> 245
 <212> PRT
 <213> Homo sapiens

 <400> 40
 Ala Ala Val Asp Ile Arg Asp Asn Leu Leu Gly Ile Ser Trp Val Asp
 1 5 10 15
 Ser Ser Trp Ile Pro Ile Leu Asn Ser Gly Ser Val Leu Asp Tyr Phe
 20 25 30
 Ser Glu Arg Ser Asn Pro Phe Tyr Asp Arg Thr Cys Asn Asn Glu Val
 35 40 45
 Val Lys Met Gln Arg Leu Thr Leu Glu His Leu Asn Gln Met Val Gly
 50 55 60
 Ile Glu Tyr Ile Leu Leu His Ala Gln Glu Pro Ile Leu Phe Ile Ile
 65 70 75 80
 Arg Lys Gln Gln Arg Gln Ser Pro Ala Gln Val Ile Pro Leu Ala Asp
 85 90 95
 Tyr Tyr Ile Ile Ala Gly Val Ile Tyr Gln Ala Pro Asp Leu Gly Ser
 100 105 110
 Val Ile Asn Ser Arg Val Leu Thr Ala Val His Gly Ile Gln Ser Ala
 115 120 125

Phe Asp Glu Ala Met Ser Tyr Cys Arg Tyr His Pro Ser Lys Gly Tyr
 130 135 140
 Trp Trp His Phe Lys Asp His Glu Glu Gln Asp Lys Val Arg Pro Lys
 145 150 155 160
 Ala Lys Arg Lys Glu Glu Pro Ser Ser Ile Phe Gln Arg Gln Arg Val
 165 170 175
 Asp Ala Leu Leu Asp Leu Arg Gln Lys Phe Pro Pro Lys Phe Val
 180 185 190
 Gln Leu Lys Pro Gly Glu Lys Pro Val Pro Val Asp Gln Thr Lys Lys
 195 200 205
 Glu Ala Glu Pro Ile Pro Glu Thr Val Lys Pro Glu Glu Lys Glu Thr
 210 215 220
 Thr Lys Asn Val Gln Gln Thr Val Ser Ala Lys Gly Pro Pro Glu Lys
 225 230 235 240
 Arg Met Arg Leu Gln
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 <210> 41
 <211> 163
 <212> PRT
 <213> Homo sapiens
 <400> 41
 Gly Glu Arg Gln Gly Leu Val Ala Arg Ala Arg Leu Ser Leu Arg Pro
 1 5 10 15
 Ser Ile Pro Glu Leu Ser Glu Arg Thr Ser Arg Pro Cys Arg Ala Ser
 20 25 30
 Pro Ala Ser Leu Pro Ser Gln His Thr Ser Ser Pro Ala Gln Ala Arg
 35 40 45
 Val Arg Asn Leu Ala Gln Ser Thr Phe Pro Leu Ala Ala Gln Glu Thr
 50 55 60
 Pro Gly Arg Ala Pro Ala His Ala Pro Leu Ser Ser Phe Val Pro Gly
 65 70 75 80
 Val Gly Gly Arg Ser Pro Ala Ser Val Gly Ile Ser Ala Pro Gly Gly
 85 90 95
 Gly Pro Ser Gly Ala Ala Ala Lys Ile Pro Leu Glu Leu Thr Gln Ser
 100 105 110
 Arg Val Gln Lys Ile Trp Val Pro Val Asp His Arg Pro Ser Leu Pro
 115 120 125
 Arg Ser Cys Gly Pro Lys Leu Thr Asn Ser Pro Ala Val Phe Val Met

130 135 140
 Val Gly Leu Pro Arg Pro Gly Gln Asp Leu Leu Leu His Glu Ser Leu
 145 150 155 160
 Leu Ala Ala

 <210> 42
 <211> 243
 <212> PRT
 <213> Homo sapiens

 <400> 42
 Val Asp Ile Arg Asp Asn Leu Leu Gly Ile Ser Trp Val Asp Ser Ser
 1 5 10 15
 Trp Ile Pro Ile Leu Asn Ser Gly Ser Val Leu Asp Tyr Phe Ser Glu
 20 25 30
 Arg Ser Asn Pro Phe Tyr Asp Arg Thr Cys Asn Asn Glu Val Val Lys
 35 40 45
 Met Gln Arg Leu Thr Leu Glu His Leu Asn Gln Met Val Gly Ile Glu
 50 55 60
 Tyr Ile Leu Leu His Ala Gln Glu Pro Ile Leu Phe Ile Ile Arg Lys
 65 70 75 80
 Gln Gln Arg Gln Ser Pro Ala Gln Val Ile Pro Leu Ala Asp Tyr Tyr
 85 90 95
 Ile Ile Ala Gly Val Ile Tyr Gln Ala Pro Asp Leu Gly Ser Val Ile
 100 105 110
 Asn Ser Arg Val Leu Thr Ala Val His Gly Ile Gln Ser Ala Phe Asp
 115 120 125
 Glu Ala Met Ser Tyr Cys Arg Tyr His Pro Ser Lys Gly Tyr Trp Trp
 130 135 140
 His Phe Lys Asp His Glu Glu Gln Asp Lys Val Arg Pro Lys Ala Lys
 145 150 155 160
 Arg Lys Glu Glu Pro Ser Ser Ile Phe Gln Arg Gln Arg Val Asp Ala
 165 170 175
 Leu Leu Leu Asp Leu Arg Gln Lys Phe Pro Pro Lys Phe Val Gln Leu
 180 185 190
 Lys Pro Gly Glu Lys Pro Val Pro Val Asp Gln Thr Lys Lys Glu Ala
 195 200 205
 Glu Pro Ile Pro Glu Thr Val Lys Pro Glu Glu Lys Glu Thr Thr Lys
 210 215 220

Asn Val Gln Gln Thr Val Ser Ala Lys Gly Pro Pro Glu Lys Arg Met
 225 230 235 240

Arg Leu Gln

<210> 43

<211> 244

<212> PRT

<213> Homo sapiens

<400> 43

Ala Val Asp Ile Arg Asp Asn Leu Leu Gly Ile Ser Trp Val Asp Ser
 1 5 10 15

Ser Trp Ile Pro Ile Leu Asn Ser Gly Ser Val Leu Asp Tyr Phe Ser
 20 25 30

Glu Arg Ser Asn Pro Phe Tyr Asp Arg Thr Cys Asn Asn Glu Val Val
 35 40 45

Lys Met Gln Arg Leu Thr Leu Glu His Leu Asn Gln Met Val Gly Ile
 50 55 60

Glu Tyr Ile Leu Leu His Ala Gln Glu Pro Ile Leu Phe Ile Ile Arg
 65 70 75 80

Lys Gln Gln Arg Gln Ser Pro Ala Gln Val Ile Pro Leu Ala Asp Tyr
 85 90 95

Tyr Ile Ile Ala Gly Val Ile Tyr Gln Ala Pro Asp Leu Gly Ser Val
 100 105 110

Ile Asn Ser Arg Val Leu Thr Ala Val His Gly Ile Gln Ser Ala Phe
 115 120 125

Asp Glu Ala Met Ser Tyr Cys Arg Tyr His Pro Ser Lys Gly Tyr Trp
 130 135 140

Trp His Phe Lys Asp His Glu Glu Gln Asp Lys Val Arg Pro Lys Ala
 145 150 155 160

Lys Arg Lys Glu Glu Pro Ser Ser Ile Phe Gln Arg Gln Arg Val Asp
 165 170 175

Ala Leu Leu Leu Asp Leu Arg Gln Lys Phe Pro Pro Lys Phe Val Gln
 180 185 190

Leu Lys Pro Gly Glu Lys Pro Val Pro Val Asp Gln Thr Lys Lys Glu
 195 200 205

Ala Glu Pro Ile Pro Glu Thr Val Lys Pro Glu Glu Lys Glu Thr Thr
 210 215 220

Lys Asn Val Gln Gln Thr Val Ser Ala Lys Gly Pro Pro Glu Lys Arg
 225 230 235 240

Met Arg Leu Gln

<210> 44

<211> 109

<212> PRT

<213> Homo sapiens

<400> 44

Glu Leu His Phe Ser Glu Phe Thr Ser Ala Val Ala Asp Met Lys Asn
 1 5 10 15

Ser Val Ala Asp Arg Asp Asn Ser Pro Ser Ser Cys Ala Gly Leu Phe
 20 25 30

Ile Ala Ser His Ile Gly Phe Asp Trp Pro Gly Val Trp Val His Leu
 35 40 45

Asp Ile Ala Ala Pro Val His Ala Gly Glu Arg Ala Thr Gly Phe Gly
 50 55 60

Val Ala Leu Leu Leu Ala Leu Phe Gly Arg Ala Ser Glu Asp Pro Leu
 65 70 75 80

Leu Asn Leu Val Ser Pro Leu Asp Cys Glu Val Asp Ala Gln Glu Gly
 85 90 95

Asp Asn Met Gly Arg Asp Ser Lys Arg Arg Arg Leu Val
 100 105

<210> 45

<211> 324

<212> PRT

<213> Homo sapiens

<400> 45

Arg Arg Pro Val Met Ala Gln Glu Thr Ala Pro Pro Cys Gly Pro Val
 1 5 10 15

Ser Arg Gly Asp Ser Pro Ile Ile Glu Lys Met Glu Lys Arg Thr Cys
 20 25 30

Ala Leu Cys Pro Glu Gly His Glu Trp Ser Gln Ile Tyr Phe Ser Pro
 35 40 45

Ser Gly Asn Ile Val Ala His Glu Asn Cys Leu Leu Tyr Ser Ser Gly
 50 55 60

Leu Val Glu Cys Glu Thr Leu Asp Leu Arg Asn Thr Ile Arg Asn Phe
 65 70 75 80

Asp Val Lys Ser Val Lys Lys Glu Ile Trp Arg Gly Arg Arg Leu Lys
 85 90 95
 Cys Ser Phe Cys Asn Lys Gly Gly Ala Thr Val Gly Cys Asp Leu Trp
 100 105 110
 Phe Cys Lys Lys Ser Tyr His Tyr Val Cys Ala Lys Lys Asp Gln Ala
 115 120 125
 Ile Leu Gln Val Asp Gly Asn His Gly Thr Tyr Lys Leu Phe Cys Pro
 130 135 140
 Glu His Ser Pro Glu Gln Glu Glu Ala Thr Glu Ser Ala Asp Asp Pro
 145 150 155 160
 Ser Met Lys Lys Lys Arg Gly Lys Asn Lys Arg Leu Ser Ser Gly Pro
 165 170 175
 Pro Ala Gln Pro Lys Thr Met Lys Cys Ser Asn Ala Lys Arg His Met
 180 185 190
 Thr Glu Glu Pro His Gly His Thr Asp Ala Ala Val Lys Ser Pro Phe
 195 200 205
 Leu Lys Lys Cys Gln Glu Ala Gly Leu Leu Thr Glu Leu Phe Glu His
 210 215 220
 Ile Leu Glu Asn Met Asp Ser Val His Gly Arg Leu Val Asp Glu Thr
 225 230 235 240
 Ala Ser Glu Ser Asp Tyr Glu Gly Ile Glu Thr Leu Leu Phe Asp Cys
 245 250 255
 Gly Leu Phe Lys Asp Thr Leu Arg Lys Phe Gln Glu Val Ile Lys Ser
 260 265 270
~~Lys Ala Cys Glu Trp Glu Glu Arg Gln Arg Gln Met Lys Gln Gln Leu~~
~~275 280 285~~
 Glu Ala Leu Ala Asp Leu Gln Gln Ser Leu Cys Ser Phe Gln Glu Asn
 290 295 300
 Gly Asp Leu Asp Cys Ser Ser Ser Thr Ser Gly Ser Leu Leu Pro Pro
 305 310 315 320
 Glu Asp His Gln

 <210> 46
 <211> 244
 <212> PRT
 <213> Homo sapiens

 <400> 46
 Ala Val Asp Ile Arg Asp Asn Leu Leu Gly Ile Ser Trp Val Asp Ser

25

1 5 10 15
 Ser Trp Ile Pro Ile Leu Asn Ser Gly Ser Val Leu Asp Tyr Phe Ser
 20 25 30
 Glu Arg Ser Asn Pro Phe Tyr Asp Arg Thr Cys Asn Asn Glu Val Val
 35 40 45
 Lys Met Gln Arg Leu Thr Leu Glu His Leu Asn Gln Met Val Gly Ile
 50 55 60
 Glu Tyr Ile Leu Leu His Ala Gln Glu Pro Ile Leu Phe Ile Ile Arg
 65 70 75 80
 Lys Gln Gln Arg Gln Ser Pro Ala Gln Val Ile Pro Leu Ala Asp Tyr
 85 90 95
 Tyr Ile Ile Ala Gly Val Ile Tyr Gln Ala Pro Asp Leu Gly Ser Val
 100 105 110
 Ile Asn Ser Arg Val Leu Thr Ala Val His Gly Ile Gln Ser Ala Phe
 115 120 125
 Asp Glu Ala Met Ser Tyr Cys Arg Tyr His Pro Ser Lys Gly Tyr Trp
 130 135 140
 Trp His Phe Lys Asp His Glu Glu Gln Asp Lys Val Arg Pro Lys Ala
 145 150 155 160
 Lys Arg Lys Glu Glu Pro Ser Ser Ile Phe Gln Arg Gln Arg Val Asp
 165 170 175
 Ala Leu Leu Leu Asp Leu Arg Gln Lys Phe Pro Pro Lys Phe Val Gln
 180 185 190
 Leu Lys Pro Gly Glu Lys Pro Val Pro Val Asp Gln Thr Lys Lys Glu
 195 200 205
 Ala Glu Pro Ile Pro Glu Thr Val Lys Pro Glu Glu Lys Glu Thr Thr
 210 215 220
 Lys Asn Val Gln Gln Thr Val Ser Ala Lys Gly Pro Pro Glu Lys Arg
 225 230 235 240
 Met Arg Leu Gln

<210> 47
 <211> 14
 <212> DNA
 <213> Homo sapiens

<400> 47
 tttttttttt ttag

<210> 48
 <211> 10
 <212> DNA
 <213> Homo sapiens

<400> 48
 cttcaacctc

10

<210> 49
 <211> 496
 <212> DNA
 <213> Homo sapiens

<400> 49
 gcaccatgta ccgagcactt cggctcctcg cgcgctcgcg tccccctcgtg cgggctccag 60
 ccgcagcctt agcttcggct cccggcttgg gtggcgcggc cgtgccctcg ttttggcctc 120
 cgaacgcggc tcgaatggca agccaaaatt ccttcgggat agaatatgat acctttgggtg 180
 aactaaagggt gccaaatgat aagtattatg gcgcccagac cgtgagatct acgatgaact 240
 ttaagattgg aggtgtgaca gaacgcattg caacccccagt tattaaagct tttggcatct 300
 tgaagcgcgc ggcgctgaa gttaaaccagg attatggctt tgatccaaag attgctaatt 360
 caataatgaa ggcagcagat gaggtagctg aaggtaaat aaatgatcat tttcctctcg 420
 tggatatggca gactggatca ggaactcaga caaatatgaa tgtaaatgaa gtcattagcc 480
 aatagagcaa ttgaaa 496

<210> 50
 <211> 499
 <212> DNA
 <213> Homo sapiens

<400> 50
 agaaaaagtc tatgtttgca gaaatacaga tccaagacaa agacaggatg ggcactgctg 60
 gaaaagtat taaatgcaaa gcagctgtgc tttgggagca gaagcaaccc ttctccattg 120
 aggaaataga agttgcccc acaaagacta aagaagttcg cattaagatt ttggccacag 180
 gaatctgtcg cacagatgac catgtgataa aaggaacaat ggtgtccaag ttccagtgga 240
 ttgtgggaca tgaggcaact gggattgtag agagcattgg agaaggagtg actacagtga 300
 aaccaggtga caaagtcatt cctctcttcc tgccacaatg tagagaatgc aatgcttgc 360
 gaaagccaga tggcaacccc tgcattagca ggcattatgc tggcctgga gtactggctg 420
 atggcaccac cagatttaca tgcaagggcg aaccagtcca ccattcatg aacaccagta 480
 catttaccga gtacacagt 499

<210> 51
 <211> 887
 <212> DNA
 <213> Homo sapiens

<400> 51
 gagtctgagc agaaaggaaa agcagccttg gcagccacgt tagaggaata caaagccaca 60
 gtggccagt accagataga gatgaatcgc ctgaaggctc agctggagaa tgaaaagcag 120
 aaagtggcag agctgtattc tatccataac tctggagaca aatctgatat tcaggacctc 180
 ctggagagtg tcaggctgga caaagaaaaa gcagagactt tggctagtag cttgcaggaa 240
 gatctggctc ataccgaaa tgatgccaat cgattacagg atgccattgc taaggtagag 300
 gatgaatacc ggccttcca agaagaagct aagaaacaaa ttgaagattc gaatatgacg 360
 ttagaaaaat taagatcaga cctggatgaa aaagaaacag aaaggagtga catgaaagaa 420
 accatctttg aacttgaaga tgaagtagaa caacatcgtg ctgtgaaact tcatgacaac 480
 ctcattatct ctgatctaga gaatacagtt aaaaaactcc aggaccaaaa gcacgacatg 540

gaaagagaaa taaagacact ccacagaaga cttcggaag aatctgcgga atggcggcag 600
tttcaggctg atctccagac tgcagtagtc attgcaaag acattaaatc tgaagcccaa 660
gaggagattg gtgatctaaa gcgccggtta catgaggctc aagaaaaaaa tgagaaactc 720
acaaaagaat tggaggaaat aaagtcacgc aagcaagagg aggagcgagg cgggtatata 780
attacatgaa tgccgttgag agagatttgg cagccttaag gcagggaatg ggactgagta 840
gaaggtcctc gacttcctca gagccaactc ctacagtaaa aaccctc 887

<210> 52

<211> 491

<212> DNA

<213> Homo sapiens

<400> 52

ggcacgagct tttccaaaaa tcatgctgct cttttctcta aagttcttac attttataga 60
aaggaacctc tcaactctga ggcctactac agctctctc aggatttgcc ctatccagat 120
cctgctatag ctacgttttc agttcagaaa gtcactctc agtctgatgg ctccagttca 180
aaagtgaag tcaaaagtgc agtaaatgtc catggcattt tcagtgtgtc cagtgcattc 240
ttagtggagg ttcacaagtc tgaggaaaat gaggagccaa tggaaacaga tcagaatgca 300
aaggaggaag agaagatgca agtggaccag gaggaaaccac atgttgaa gaacacagcag 360
cagacaccag gcagaaaata aggcagagtc tgaagaaatg gagacctctc aagctggatc 420
caaggataaa aagatggacc aaccacccca agccaagaag gcaaaagtga agaccagtac 480
tgtggacctg g 491

<210> 53

<211> 787

<212> DNA

<213> Homo sapiens

<400> 53

aagcagttga gtaggcagaa aaaagaacct cttcattaag gattaaaatg tataggccag 60
cacgtgtaac ttcgacttca agatttctga atccatattg agtatgtttc attgtcgctg 120
caggggtagt gatcctggca gtcaccatag ctctacttgt ttacttttta gcttttgatc 180
aaaaatctta cttttatagg agcagtttcc aactcctaaa tgttgaatgt aatagtcagt 240
taaattcacc agctacacag gaatacagga ctttgagtgg aagaattgaa tctctgatta 300
ctaaaacatt caaagaatca aatttaagaa atcagttcat cagagctcat gttgccaaac 360
tgaggcaaga tggtagtggt gtgagagcgg atgtgtgcat gaaatttcaa ttcactagaa 420
ataacaatgg agcatcaatg aaaagcagaa ttgagtctgt ttacgacaa atgctgaata 480
actctggaaa cctggaaata aacccttcaa ctgagataac atcacttact gaccaggctg 540
cagcaaatg gcttattaat gaatgtgggg ccggtccaga cctaataaca ttgtctgagc 600
agagaatcct tggaggcact gaggctgagg agggagagctg gccgtggcaa gtcagctctg 660
ggctcaataa tgcccaccac tgtggaggca gcctgatcaa taacatgtgg atcctgacag 720
cagctcactg cttcagaagc aactctaate ctgctgactg gattgccacg tctgggtattt 780
ccacaac 787

<210> 54

<211> 386

<212> DNA

<213> Homo sapiens

<400> 54

ggcattttca gtgtgtccag tgcattctta gtggagggtc acaagtctga ggaaaatgag 60
gagccaatgg aaacagatca gaatgcaaag gaggaagaga agatgcaagt ggaccaggag 120
gaaccacatg ttgaagagca acagcagcag acaccagcag aaaataaggc agagtctgaa 180
gaaatggaga cctctcaagc tggatccaag gataaaaaga tggaccaacc accccaagcc 240
aagaaggcaa aagtgaagac cagtactgtg gacctgccaa tcgagaatca gctattatgg 300

cagatagaca gagagatgct caacttgtag attgaaaatg agggtaagat gatcatgcag 360
gataaactgg agaaggagcg gaatga 386

<210> 55
<211> 1462
<212> DNA
<213> Homo sapiens

<400> 55
aagcagttga gtaggcagaa aaaagaacct ctctattaag gattaaaatg tataggccag 60
cacgtgtaac ttcgacttca agatttctga atccatatgt agtatgtttc attgtcgtcg 120
caggggtagt gatcctggca gtcaccatag ctctacttgt ttacttttta gcttttgatc 180
aaaaatctta cttttrtagg agcagttttc aactcctaaa tgttgaatat aatagtcagt 240
taaattcacc agctacacag gaatacagga ctttgagtgg aagaattgaa tctctgatta 300
ctaaaacatt caaagaatca aatttaagaa atcagttcat cagagctcat gttgccaaac 360
tgaggcaaga tggtagtggg gtgagagcgg atgttgtcat gaaatttcaa ttcactagaa 420
ataacaatgg agcatcaatg aaaagcagaa ttgagtctgt tttacgacaa atgctgaata 480
actctggaaa cctggaaata aacccttcaa ctgagataac atcacttact gaccaggctg 540
cagcaaattg gcttattaat gaatgtgggg ccggtccaga cctaataaca ttgtctgagc 600
agagaatcct tggaggcact gaggtgagg agggaagctg gccgtggcaa gtcagctctg 660
ggctcaataa tgcccaccac tgtggaggca gcctgatcaa taacatgtgg atcctgacag 720
cagctcactg cttcagaagc aacttcaatc ctctgtactg gattgccacg tctggtattt 780
ccacaacatt tcctaaacta agaatgagag taagaaatat ttttaattcat aacaattata 840
aatctgcaac tcctgaaaat gacattgcac ttgtgagact tgagaacagt gtcaccttta 900
ccaaagatat ccatagtgtg tgtctcccag ctgctaccca gaatattcca cctggctcta 960
ctgcttatgt aacaggatgg ggcgctcaag aatatgctgg ccacacagtt ccagagctaa 1020
ggcaaggaca ggtcagaata ataagtaatg atgratgtaa tgcaccacat agttataatg 1080
gagccatcct gtctggaatg ctgtgtgctg gagtacctca aggtggagtg gacgcatgtc 1140
aggggtgactc tgggtggccca ctagtacaag aagactcacg gcggctttgg tttattgtgg 1200
ggatagtaag ctggggagat cagtgtggcc tgccggataa gccaggagtg tatactcgag 1260
tgacagcata cattgactgg attaggcaac aaactgggat ctagtgaac aagtgcattc 1320
ctgttgcaaa gtctgtatgc aggtgtgctt gtcttaaat ccaaagcttt acatttcaac 1380
tgaaaaagaa actagaaatg tcctaattta acatcttgtt acataaatat ggtttaacaa 1440
aaaaaaaaa aaaaaactcg ag 1462

<210> 56
<211> 159
<212> PRT
<213> Homo sapiens

<400> 56
Thr Met Tyr Arg Ala Leu Arg Leu Leu Ala Arg Ser Arg Pro Leu Val
1 5 10 15
Arg Ala Pro Ala Ala Ala Leu Ala Ser Ala Pro Gly Leu Gly Gly Ala
20 25 30
Ala Val Pro Ser Phe Trp Pro Pro Asn Ala Ala Arg Met Ala Ser Gln
35 40 45
Asn Ser Phe Arg Ile Glu Tyr Asp Thr Phe Gly Glu Leu Lys Val Pro
50 55 60
Asn Asp Lys Tyr Tyr Gly Ala Gln Thr Val Arg Ser Thr Met Asn Phe
65 70 75 80

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<210> 58
 <211> 259
 <212> PRT
 <213> Homo sapiens

<400> 58
 Glu Ser Glu Gln Lys Gly Lys Ala Ala Leu Ala Ala Thr Leu Glu Glu
 1 5 10 15
 Tyr Lys Ala Thr Val Ala Ser Asp Gln Ile Glu Met Asn Arg Leu Lys
 20 25 30
 Ala Gln Leu Glu Asn Glu Lys Gln Lys Val Ala Glu Leu Tyr Ser Ile
 35 40 45
 His Asn Ser Gly Asp Lys Ser Asp Ile Gln Asp Leu Leu Glu Ser Val
 50 55 60
 Arg Leu Asp Lys Glu Lys Ala Glu Thr Leu Ala Ser Ser Leu Gln Glu
 65 70 75 80
 Asp Leu Ala His Thr Arg Asn Asp Ala Asn Arg Leu Gln Asp Ala Ile
 85 90 95
 Ala Lys Val Glu Asp Glu Tyr Arg Ala Phe Gln Glu Glu Ala Lys Lys
 100 105 110
 Gln Ile Glu Asp Leu Asn Met Thr Leu Glu Lys Leu Arg Ser Asp Leu
 115 120 125
 Asp Glu Lys Glu Thr Glu Arg Ser Asp Met Lys Glu Thr Ile Phe Glu
 130 135 140
 Leu Glu Asp Glu Val Glu Gln His Arg Ala Val Lys Leu His Asp Asn
 145 150 155 160
 Leu Ile Ile Ser Asp Leu Glu Asn Thr Val Lys Lys Leu Gln Asp Gln
 165 170 175
 Lys His Asp Met Glu Arg Glu Ile Lys Thr Leu His Arg Arg Leu Arg
 180 185 190
 Glu Glu Ser Ala Glu Trp Arg Gln Phe Gln Ala Asp Leu Gln Thr Ala
 195 200 205
 Val Val Ile Ala Asn Asp Ile Lys Ser Glu Ala Gln Glu Glu Ile Gly
 210 215 220
 Asp Leu Lys Arg Arg Leu His Glu Ala Gln Glu Lys Asn Glu Lys Leu
 225 230 235 240
 Thr Lys Glu Leu Glu Glu Ile Lys Ser Arg Lys Gln Glu Glu Glu Arg
 245 250 255

Gly Gly Tyr

<210> 59

<211> 125

<212> PRT

<213> Homo sapiens

<400> 59

Gly Thr Ser Phe Ser Lys Asn His Ala Ala Pro Phe Ser Lys Val Leu
 1 5 10 15
 Thr Phe Tyr Arg Lys Glu Pro Phe Thr Leu Glu Ala Tyr Tyr Ser Ser
 20 25 30
 Pro Gln Asp Leu Pro Tyr Pro Asp Pro Ala Ile Ala Gln Phe Ser Val
 35 40 45
 Gln Lys Val Thr Pro Gln Ser Asp Gly Ser Ser Ser Lys Val Lys Val
 50 55 60
 Lys Val Arg Val Asn Val His Gly Ile Phe Ser Val Ser Ser Ala Ser
 65 70 75 80
 Leu Val Glu Val His Lys Ser Glu Glu Asn Glu Glu Pro Met Glu Thr
 85 90 95
 Asp Gln Asn Ala Lys Glu Glu Glu Lys Met Gln Val Asp Gln Glu Glu
 100 105 110
 Pro His Val Glu Glu Gln Gln Gln Gln Thr Pro Gly Arg
 115 120 125

<210> 60

<211> 246

<212> PRT

<213> Homo sapiens

<400> 60

Met Tyr Arg Pro Ala Arg Val Thr Ser Thr Ser Arg Phe Leu Asn Pro
 1 5 10 15
 Tyr Val Val Cys Phe Ile Val Val Ala Gly Val Val Ile Leu Ala Val
 20 25 30
 Thr Ile Ala Leu Leu Val Tyr Phe Leu Ala Phe Asp Gln Lys Ser Tyr
 35 40 45
 Phe Tyr Arg Ser Ser Phe Gln Leu Leu Asn Val Glu Tyr Asn Ser Gln
 50 55 60
 Leu Asn Ser Pro Ala Thr Gln Glu Tyr Arg Thr Leu Ser Gly Arg Ile
 65 70 75 80

Glu Ser Leu Ile Thr Lys Thr Phe Lys Glu Ser Asn Leu Arg Asn Gln
 85 90 95
 Phe Ile Arg Ala His Val Ala Lys Leu Arg Gln Asp Gly Ser Gly Val
 100 105 110
 Arg Ala Asp Val Val Met Lys Phe Gln Phe Thr Arg Asn Asn Asn Gly
 115 120 125
 Ala Ser Met Lys Ser Arg Ile Glu Ser Val Leu Arg Gln Met Leu Asn
 130 135 140
 Asn Ser Gly Asn Leu Glu Ile Asn Pro Ser Thr Glu Ile Thr Ser Leu
 145 150 155 160
 Thr Asp Gln Ala Ala Ala Asn Trp Leu Ile Asn Glu Cys Gly Ala Gly
 165 170 175
 Pro Asp Leu Ile Thr Leu Ser Glu Gln Arg Ile Leu Gly Gly Thr Glu
 180 185 190
 Ala Glu Glu Gly Ser Trp Pro Trp Gln Val Ser Leu Arg Leu Asn Asn
 195 200 205
 Ala His His Cys Gly Gly Ser Leu Ile Asn Asn Met Trp Ile Leu Thr
 210 215 220
 Ala Ala His Cys Phe Arg Ser Asn Ser Asn Pro Arg Asp Trp Ile Ala
 225 230 235 240
 Thr Ser Gly Ile Ser Thr
 245

<210> 61

<211> 128

<212> PRT

<213> Homo sapiens

<400> 61

Gly Ile Phe Ser Val Ser Ser Ala Ser Leu Val Glu Val His Lys Ser
 1 5 10 15

Glu Glu Asn Glu Glu Pro Met Glu Thr Asp Gln Asn Ala Lys Glu Glu
 20 25 30

Glu Lys Met Gln Val Asp Gln Glu Glu Pro His Val Glu Glu Gln Gln
 35 40 45

Gln Gln Thr Pro Ala Glu Asn Lys Ala Glu Ser Glu Glu Met Glu Thr
 50 55 60

Ser Gln Ala Gly Ser Lys Asp Lys Lys Met Asp Gln Pro Pro Gln Ala
 65 70 75 80

Lys Lys Ala Lys Val Lys Thr Ser Thr Val Asp Leu Pro Ile Glu Asn

85 90 95
 Gln Leu Leu Trp Gln Ile Asp Arg Glu Met Leu Asn Leu Tyr Ile Glu
 100 105 110
 Asn Glu Gly Lys Met Ile Met Gln Asp Lys Leu Glu Lys Glu Arg Asn
 115 120 125

 <210> 62
 <211> 418
 <212> PRT
 <213> Homo sapiens

 <400> 62
 Met Tyr Arg Pro Ala Arg Val Thr Ser Thr Ser Arg Phe Leu Asn Pro
 1 5 10 15
 Tyr Val Val Cys Phe Ile Val Val Ala Gly Val Val Ile Leu Ala Val
 20 25 30
 Thr Ile Ala Leu Leu Val Tyr Phe Leu Ala Phe Asp Gln Lys Ser Tyr
 35 40 45
 Phe Tyr Arg Ser Ser Phe Gln Leu Leu Asn Val Glu Tyr Asn Ser Gln
 50 55 60
 Leu Asn Ser Pro Ala Thr Gln Glu Tyr Arg Thr Leu Ser Gly Arg Ile
 65 70 75 80
 Glu Ser Leu Ile Thr Lys Thr Phe Lys Glu Ser Asn Leu Arg Asn Gln
 85 90 95
 Phe Ile Arg Ala His Val Ala Lys Leu Arg Gln Asp Gly Ser Gly Val
 100 105 110
 Arg Ala Asp Val Val Met Lys Phe Gln Phe Thr Arg Asn Asn Asn Gly
 115 120 125
 Ala Ser Met Lys Ser Arg Ile Glu Ser Val Leu Arg Gln Met Leu Asn
 130 135 140
 Asn Ser Gly Asn Leu Glu Ile Asn Pro Ser Thr Glu Ile Thr Ser Leu
 145 150 155 160
 Thr Asp Gln Ala Ala Ala Asn Trp Leu Ile Asn Glu Cys Gly Ala Gly
 165 170 175
 Pro Asp Leu Ile Thr Leu Ser Glu Gln Arg Ile Leu Gly Gly Thr Glu
 180 185 190
 Ala Glu Glu Gly Ser Trp Pro Trp Gln Val Ser Leu Arg Leu Asn Asn
 195 200 205
 Ala His His Cys Gly Gly Ser Leu Ile Asn Asn Met Trp Ile Leu Thr

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210 215 220
 Ala Ala His Cys Phe Arg Ser Asn Ser Asn Pro Arg Asp Trp Ile Ala
 225 230 235 240
 Thr Ser Gly Ile Ser Thr Thr Phe Pro Lys Leu Arg Met Arg Val Arg
 245 250 255
 Asn Ile Leu Ile His Asn Asn Tyr Lys Ser Ala Thr His Glu Asn Asp
 260 265 270
 Ile Ala Leu Val Arg Leu Glu Asn Ser Val Thr Phe Thr Lys Asp Ile
 275 280 285
 His Ser Val Cys Leu Pro Ala Ala Thr Gln Asn Ile Pro Pro Gly Ser
 290 295 300
 Thr Ala Tyr Val Thr Gly Trp Gly Ala Gln Glu Tyr Ala Gly His Thr
 305 310 315 320
 Val Pro Glu Leu Arg Gln Gly Gln Val Arg Ile Ile Ser Asn Asp Val
 325 330 335
 Cys Asn Ala Pro His Ser Tyr Asn Gly Ala Ile Leu Ser Gly Met Leu
 340 345 350
 Cys Ala Gly Val Pro Gln Gly Gly Val Asp Ala Cys Gln Gly Asp Ser
 355 360 365
 Gly Gly Pro Leu Val Gln Glu Asp Ser Arg Arg Leu Trp Phe Ile Val
 370 375 380
 Gly Ile Val Ser Trp Gly Asp Gln Cys Gly Leu Pro Asp Lys Pro Gly
 385 390 395 400
 Val Tyr Thr Arg Val Thr Ala Tyr Ile Asp Trp Ile Arg Gln Gln Thr
 405 410 415
 Gly Ile

<210> 63
 <211> 776
 <212> DNA
 <213> Homo sapiens

<400> 63
 cacagatggt gatagaggaa tccatcttgc agtcagataa agccctcact gatagagaga 60
 aggcagtagc agtggatcgg gccaaagaagg aggcagctga gaaggaacag gaacttttaa 120
 aacagaaatt acaggagcag ccagcaacag atggaggctc aagataagag tcgcaaggaa 180
 aactagccaa ctgaaggaga agctgcagat ggagagagaa cacctactga gagagcagat 240
 tatgatgttg gagcacacgc agaaggtcca aaatgattgg cttcatgaag gatttaagaa 300
 gaagtatgag gagatgaatg cagagataag tcaatttaaa cgtatgattg atactacaaa 360
 aaatgatgat actccctgga ttgcacgaac cttggacaac cttgccgatg agctaactgc 420
 aatattgtct gtccttgcta aattaattgg tcatgggtgc aaaggtgtga gctcactctt 480

taaaaagcat aagctcccct ttttaaggata ttatagattg tacatatatg ctttggacta 540
 tttttgatct gtatgttttt ctttttcatt cagcaagttt tttttttttt tcagagtctt 600
 actctgttgc ccaggctgga gtacagtggg gcaatctcag ctcaactgcaa cctctgcctc 660
 ctgggttcaa gagattcacc tgcctcagcc ccctagtagc tgggattata ggtgtacacc 720
 accacaccca gctaattttt gtatttttag tagagatggg gtttcactat gttggc 776

<210> 64

<211> 160

<212> DNA

<213> Homo sapiens

<400> 64

gcagcgctct cgggtgcagt acccaactgga aggacttagg cgctcgctg gacaccgcaa 60
 gccctcagt agcctcggcc caagaggcct gctttccact cgctagcccc gccggggggtc 120
 cgtgtcctgt ctcggtggcc ggacccgggc ccgagcccgga 160

<210> 65

<211> 72

<212> PRT

<213> Homo sapiens

<400> 65

Leu Ser Ala Met Gly Phe Thr Ala Ala Gly Ile Ala Ser Ser Ser Ile
 1 5 10 15

Ala Ala Lys Met Met Ser Ala Ala Ala Ile Ala Asn Gly Gly Gly Val
 20 25 30

Ala Ser Gly Ser Leu Val Ala Thr Leu Gln Ser Leu Gly Ala Thr Gly
 35 40 45

Leu Ser Gly Leu Thr Lys Phe Ile Leu Gly Ser Ile Gly Ser Ala Ile
 50 55 60

Ala Ala Val Ile Ala Arg Phe Tyr
 65 70

<210> 66

<211> 2581

<212> DNA

<213> Homo sapiens

<400> 66

ctttcaaccc gcgctgcgag gctccagccc cgcgcgcccc cacccttgc cctcccgagg 60
 gctccgcagg gtgagggtggc tttgacccc gggtgcccgg ccagcacgac cgaggagggtg 120
 gctggacagc tggaggatga acggagaagc cgactgcccc acagacctgg aaatggccgc 180
 ccccaaaggc caagaccgtt ggtcccagga agacatgctg actttgctgg aatgcatgaa 240
 gaacaacctt ccattccaatg acagctccaa gttcaaaacc accgaatcac acatggactg 300
 ggaaaaagta gcattttaaag acttttctgg agacatgtgc aagctcaaata ggggtggagat 360
 ttctaattgag gtgaggaagt tccgtacatt gacagaattg atcctcgatg ctcaaggaaca 420
 tgtaaaaaat cettacaaag gcaaaaaact caagaaacac ccagacttcc caaagaagcc 480
 cctgacccct tatttccgct tttcatgga gaagcggggc aagtatgca aactccaccc 540
 tgagatgagc aacctggacc taaccaagat tctgtccaag aaatacaagg agcttccgga 600
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<210> 67

<211> 764

<212> PRT

<213> Homo sapiens

<400> 67

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Met Asn Gly Glu Ala Asp Cys Pro Thr Asp Leu Glu Met Ala Ala Pro
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Lys Gly Gln Asp Arg Trp Ser Gln Glu Asp Met Leu Thr Leu Leu Glu
  20                      25                      30

```

```

Cys Met Lys Asn Asn Leu Pro Ser Asn Asp Ser Ser Lys Phe Lys Thr
  35                      40                      45

```

```

Thr Glu Ser His Met Asp Trp Glu Lys Val Ala Phe Lys Asp Phe Ser
  50                      55                      60

```

```

Gly Asp Met Cys Lys Leu Lys Trp Val Glu Ile Ser Asn Glu Val Arg
  65                      70                      75                      80

```


370 375 380
 Lys Gln Ala Thr Ser Pro Ala Ser Lys Lys Pro Ala Gln Glu Gly Gly
 385 390 395 400
 Lys Gly Gly Ser Glu Lys Pro Lys Arg Pro Val Ser Ala Met Phe Ile
 405 410 415
 Phe Ser Glu Glu Lys Arg Arg Gln Leu Gln Glu Glu Arg Pro Glu Leu
 420 425 430
 Ser Glu Ser Glu Leu Thr Arg Leu Leu Ala Arg Met Trp Asn Asp Leu
 435 440 445
 Ser Glu Lys Lys Lys Ala Lys Tyr Lys Ala Arg Glu Ala Ala Leu Lys
 450 455 460
 Ala Gln Ser Glu Arg Lys Pro Gly Gly Glu Arg Glu Glu Arg Gly Lys
 465 470 475 480
 Leu Pro Glu Ser Pro Lys Arg Ala Glu Glu Ile Trp Gln Gln Ser Val
 485 490 495
 Ile Gly Asp Tyr Leu Ala Arg Phe Lys Asn Asp Arg Val Lys Ala Leu
 500 505 510
 Lys Ala Met Glu Met Thr Trp Asn Asn Met Glu Lys Lys Glu Lys Leu
 515 520 525
 Met Trp Ile Lys Lys Ala Ala Glu Asp Gln Lys Arg Tyr Glu Arg Glu
 530 535 540
 Leu Ser Glu Met Arg Ala Pro Pro Ala Ala Thr Asn Ser Ser Lys Lys
 545 550 555 560
 Met Lys Phe Gln Gly Glu Pro Lys Lys Pro Pro Met Asn Gly Tyr Gln
 565 570 575
 Lys Phe Ser Gln Glu Leu Leu Ser Asn Gly Glu Leu Asn His Leu Pro
 580 585 590
 Leu Lys Glu Arg Met Val Glu Ile Gly Ser Arg Trp Gln Arg Ile Ser
 595 600 605
 Gln Ser Gln Lys Glu His Tyr Lys Lys Leu Ala Glu Glu Gln Gln Lys
 610 615 620
 Gln Tyr Lys Val His Leu Asp Leu Trp Val Lys Ser Leu Ser Pro Gln
 625 630 635 640
 Asp Arg Ala Ala Tyr Lys Glu Tyr Ile Ser Asn Lys Arg Lys Ser Met
 645 650 655
 Thr Lys Leu Arg Gly Pro Asn Pro Lys Ser Ser Arg Thr Thr Leu Gln
 660 665 670

Ser Lys Ser Glu Ser Glu Glu Asp Asp Glu Glu Asp Glu Asp Asp Glu
 675 680 685

Asp Glu Asp Glu Glu Glu Glu Asp Asp Glu Asn Gly Asp Ser Ser Glu
 690 695 700

Asp Gly Gly Asp Ser Ser Glu Ser Ser Ser Glu Asp Glu Ser Glu Asp
 705 710 715 720

Gly Asp Glu Asn Glu Glu Asp Asp Glu Asp Glu Asp Asp Asp Glu Asp
 725 730 735

Asp Asp Glu Asp Glu Asp Asn Glu Ser Glu Gly Ser Ser Ser Ser Ser
 740 745 750

Ser Ser Leu Gly Asp Ser Ser Asp Phe Asp Ser Asn
 755 760

<210> 68
 <211> 434
 <212> DNA
 <213> Homo sapiens

<400> 68
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<210> 69
 <211> 244
 <212> DNA
 <213> Homo sapiens

<400> 69
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 ttatgtgctg accttccctc cactattgtc ctgtgacctt gccaaatccc cctttgtgag 180
 aaacacccaa gaatgatcaa taaaaataa attaatattg gaaaaaaaaa aaaaaaaact 240
 cgag 244

<210> 70
 <211> 437
 <212> DNA
 <213> Homo sapiens

<400> 70
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tctcgcagca gcagaccttg cccgtgatga gcggggaggc ccttggctgg ctgggccagg 360
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437

<210> 71

<211> 271

<212> DNA

<213> Homo sapiens

<400> 71

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gaccaatcca aggagggtct caggaggagac ttcaggtgac cctccagggg actaccgaga 180
gttttgcaca aaagtttgtg gtgaactttt cagaacagct tcaatggaga tgacttggcc 240
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271

<210> 72

<211> 290

<212> DNA

<213> Homo sapiens

<400> 72

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cgggtggccga ggggtcccagc tcctgcttct ggcggaacgt gatcagcgag agggagcgca 180
ggaagcggat gtcgttgagc tgtgagcgtc tgcgggacct gctgccccag ttcgatggcc 240
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290

<210> 73

<211> 144

<212> PRT

<213> Homo sapiens

<400> 73

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Lys Met Leu Asp Ala Glu Asp Ile Val Gly Thr Ala Arg Pro Asp Glu
  1             5             10             15

```

```

Lys Ala Ile Met Thr Tyr Val Ser Ser Phe Tyr His Ala Phe Ser Gly
      20             25             30

```

```

Ala Gln Lys Ala Glu Thr Ala Ala Asn Arg Ile Cys Lys Val Leu Ala
      35             40             45

```

```

Val Asn Gln Glu Asn Glu Gln Leu Met Glu Asp Tyr Glu Lys Leu Ala
      50             55             60

```

```

Ser Asp Leu Leu Glu Trp Ile Arg Arg Thr Ile Pro Trp Leu Glu Asn
      65             70             75             80

```

```

Arg Val Pro Glu Asn Thr Met His Ala Met Gln Gln Lys Leu Glu Asp
      85             90             95

```

Phe Arg Asp Tyr Arg Arg Leu His Lys Pro Pro Lys Val Gln Glu Lys
 100 105 110

Cys Gln Leu Glu Ile Asn Phe Asn Thr Leu Gln Thr Lys Leu Arg Leu
 115 120 125

Ser Asn Arg Pro Ala Phe Met Pro Ser Glu Gly Arg Met Val Ser Asp
 130 135 140

<210> 74

<211> 64

<212> PRT

<213> Homo sapiens

<400> 74

Gly Ser Met Leu Val Glu Ser His His His Ser Leu Ile Ser Ser Thr
 1 5 10 15

Gln Gly His Lys His Cys Gly Arg Pro Gln Gly Pro Leu Pro Arg Lys
 20 25 30

Thr Arg Asp Leu Cys Ser Leu Val Tyr Val Leu Thr Phe Pro Pro Leu
 35 40 45

Leu Ser Cys Asp Pro Ala Lys Ser Pro Phe Val Arg Asn Thr Gln Glu
 50 55 60

<210> 75

<211> 145

<212> PRT

<213> Homo sapiens

<400> 75

Gly Thr Gly Ala Ser Ser Gly Thr Arg Thr Pro Asp Val Lys Ala Phe
 1 5 10 15

Leu Glu Ser Pro Trp Ser Leu Asp Pro Ala Ser Ala Ser Pro Glu Pro
 20 25 30

Val Pro His Ile Leu Ala Ser Ser Arg Gln Trp Asp Pro Ala Ser Cys
 35 40 45

Thr Ser Leu Gly Thr Asp Lys Cys Glu Ala Leu Leu Gly Leu Cys Gln
 50 55 60

Val Arg Gly Gly Leu Pro Pro Phe Ser Glu Pro Ser Ser Leu Val Pro
 65 70 75 80

Trp Pro Pro Gly Arg Ser Leu Pro Lys Ala Val Arg Pro Pro Leu Ser
 85 90 95

Trp Pro Pro Phe Ser Gln Gln Gln Thr Leu Pro Val Met Ser Gly Glu
 100 105 110

Ala Leu Gly Trp Leu Gly Gln Ala Gly Ser Leu Ala Met Gly Ala Ala
115 120 125

Pro Leu Gly Glu Pro Ala Lys Glu Asp Pro Met Leu Ala Gln Glu Ala
130 135 140

Gly
145

<210> 76
<211> 69
<212> PRT
<213> Homo sapiens

<400> 76
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Pro Glu Ile Glu Glu Met Ala Leu Phe Ser Ala Gln Ser Pro Tyr Ile
20 25 30

Asn Pro Ile Ile Pro Phe Thr Gly Pro Ile Gln Gly Gly Leu Gln Glu
35 40 45

Gly Leu Gln Val Thr Leu Gln Gly Thr Thr Glu Ser Phe Ala Gln Lys
50 55 60

Phe Val Val Asn Phe
65

<210> 77
<211> 96
<212> PRT
<213> Homo sapiens

<400> 77
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1 5 10 15

Gly Ser Leu Ser Gly Ala Leu Ser Cys Cys Glu Asp Ser Ala Gln Gly
20 25 30

Ser Gly Pro Pro Lys Ala Pro Thr Val Ala Glu Gly Pro Ser Ser Cys
35 40 45

Leu Arg Arg Asn Val Ile Ser Glu Arg Glu Arg Arg Lys Arg Met Ser
50 55 60

Leu Ser Cys Glu Arg Leu Arg Ala Leu Leu Pro Gln Phe Asp Gly Arg
65 70 75 80

Arg Glu Asp Met Ala Ser Val Leu Glu Met Ser Val Ala Ile Pro Ala

85

90

95

<210> 78
<211> 2076
<212> DNA
<213> Homo sapiens

<400> 78

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<210> 79
<211> 2790
<212> DNA
<213> Homo sapiens

<400> 79

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caggggtagt gatcctggca gtcaccatag cttacttgtt ttacttttta gcttttgatc 180
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<210> 80

<211> 1460

<212> DNA

<213> Homo sapiens

<400> 80

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caactgaaaa agaaactaga aatgtcctaa tttacatct tgttacataa atatggttta 1440
acaaaaaaaa aaaaaaaaaa

```

1460

<210> 81

<211> 386

<212> PRT

<213> Homo sapiens

<400> 81

```

Met Phe Ala Glu Ile Gln Ile Gln Asp Lys Asp Arg Met Gly Thr Ala
  1             5             10             15

```

```

Gly Lys Val Ile Lys Cys Lys Ala Ala Val Leu Trp Glu Gln Lys Gln
      20             25             30

```

```

Pro Phe Ser Ile Glu Glu Ile Glu Val Ala Pro Pro Lys Thr Lys Glu
      35             40             45

```

```

Val Arg Ile Lys Ile Leu Ala Thr Gly Ile Cys Arg Thr Asp Asp His
      50             55             60

```

```

Val Ile Lys Gly Thr Met Val Ser Lys Phe Pro Val Ile Val Gly His
      65             70             75             80

```

```

Glu Ala Thr Gly Ile Val Glu Ser Ile Gly Glu Gly Val Thr Thr Val
      85             90             95

```

```

Lys Pro Gly Asp Lys Val Ile Pro Leu Phe Leu Pro Gln Cys Arg Glu
      100            105            110

```

```

Cys Asn Ala Cys Arg Asn Pro Asp Gly Asn Leu Cys Ile Arg Ser Asp
      115            120            125

```

```

Ile Thr Gly Arg Gly Val Leu Ala Asp Gly Thr Thr Arg Phe Thr Cys
      130            135            140

```

```

Lys Gly Lys Pro Val His His Phe Met Asn Thr Ser Thr Phe Thr Glu

```

145 150 155 160
 Tyr Thr Val Val Asp Glu Ser Ser Val Ala Lys Ile Asp Asp Ala Ala
 165 170 175
 Pro Pro Glu Lys Val Cys Leu Ile Gly Cys Gly Phe Ser Thr Gly Tyr
 180 185 190
 Gly Ala Ala Val Lys Thr Gly Lys Val Lys Pro Gly Ser Thr Cys Val
 195 200 205
 Val Phe Gly Leu Arg Gly Val Gly Leu Ser Val Ile Met Gly Cys Lys
 210 215 220
 Ser Ala Gly Ala Ser Arg Ile Ile Gly Ile Asp Leu Asn Lys Asp Lys
 225 230 235 240
 Phe Glu Lys Ala Met Ala Val Gly Ala Thr Glu Cys Ile Ser Pro Lys
 245 250 255
 Asp Ser Thr Lys Pro Ile Ser Glu Val Leu Ser Glu Met Thr Gly Asn
 260 265 270
 Asn Val Gly Tyr Thr Phe Glu Val Ile Gly His Leu Glu Thr Met Ile
 275 280 285
 Asp Ala Leu Ala Ser Cys His Met Asn Tyr Gly Thr Ser Val Val Val
 290 295 300
 Gly Val Pro Pro Ser Ala Lys Met Leu Thr Tyr Asp Pro Met Leu Leu
 305 310 315 320
 Phe Thr Gly Arg Thr Trp Lys Gly Cys Val Phe Gly Gly Leu Lys Ser
 325 330 335
 Arg Asp Asp Val Pro Lys Leu Val Thr Glu Phe Leu Ala Lys Lys Phe
 340 345 350
 Asp Leu Asp Gln Leu Ile Thr His Val Leu Pro Phe Lys Lys Ile Ser
 355 360 365
 Glu Gly Phe Glu Leu Leu Asn Ser Gly Gln Ser Ile Arg Thr Val Leu
 370 375 380
 Thr Phe
 385

<210> 82

<211> 418

<212> PRT

<213> Homo sapiens

<400> 82

Met Tyr Arg Pro Ala Arg Val Thr Ser Thr Ser Arg Phe Leu Asn Pro

1 5 10 15
 Tyr Val Val Cys Phe Ile Val Val Ala Gly Val Val Ile Leu Ala Val
 20 25 30
 Thr Ile Ala Leu Leu Val Tyr Phe Leu Ala Phe Asp Gln Lys Ser Tyr
 35 40 45
 Phe Tyr Arg Ser Ser Phe Gln Leu Leu Asn Val Glu Tyr Asn Ser Gln
 50 55 60
 Leu Asn Ser Pro Ala Thr Gln Glu Tyr Arg Thr Leu Ser Gly Arg Ile
 65 70 75 80
 Glu Ser Leu Ile Thr Lys Thr Phe Lys Glu Ser Asn Leu Arg Asn Gln
 85 90 95
 Phe Ile Arg Ala His Val Ala Lys Leu Arg Gln Asp Gly Ser Gly Val
 100 105 110
 Arg Ala Asp Val Val Met Lys Phe Gln Phe Thr Arg Asn Asn Asn Gly
 115 120 125
 Ala Ser Met Lys Ser Arg Ile Glu Ser Val Leu Arg Gln Met Leu Asn
 130 135 140
 Asn Ser Gly Asn Leu Glu Ile Asn Pro Ser Thr Glu Ile Thr Ser Leu
 145 150 155 160
 Thr Asp Gln Ala Ala Ala Asn Trp Leu Ile Asn Glu Cys Gly Ala Gly
 165 170 175
 Pro Asp Leu Ile Thr Leu Ser Glu Gln Arg Ile Leu Gly Gly Thr Glu
 180 185 190
 Ala Glu Glu Gly Ser Trp Pro Trp Gln Val Ser Leu Arg Leu Asn Asn
 195 200 205
 Ala His His Cys Gly Gly Ser Leu Ile Asn Asn Met Trp Ile Leu Thr
 210 215 220
 Ala Ala His Cys Phe Arg Ser Asn Ser Asn Pro Arg Asp Trp Ile Ala
 225 230 235 240
 Thr Ser Gly Ile Ser Thr Thr Phe Pro Lys Leu Arg Met Arg Val Arg
 245 250 255
 Asn Ile Leu Ile His Asn Asn Tyr Lys Ser Ala Thr His Glu Asn Asp
 260 265 270
 Ile Ala Leu Val Arg Leu Glu Asn Ser Val Thr Phe Thr Lys Asp Ile
 275 280 285
 His Ser Val Cys Leu Pro Ala Ala Thr Gln Asn Ile Pro Pro Gly Ser
 290 295 300

Thr Ala Tyr Val Thr Gly Trp Gly Ala Gln Glu Tyr Ala Gly His Thr
305 310 315 320

Val Pro Glu Leu Arg Gln Gly Gln Val Arg Ile Ile Ser Asn Asp Val
325 330 335

Cys Asn Ala Pro His Ser Tyr Asn Gly Ala Ile Leu Ser Gly Met Leu
340 345 350

Cys Ala Gly Val Pro Gln Gly Gly Val Asp Ala Cys Gln Gly Asp Ser
355 360 365

Gly Gly Pro Leu Val Gln Glu Asp Ser Arg Arg Leu Trp Phe Ile Val
370 375 380

Gly Ile Val Ser Trp Gly Asp Gln Cys Gly Leu Pro Asp Lys Pro Gly
385 390 395 400

Val Tyr Thr Arg Val Thr Ala Tyr Leu Asp Trp Ile Arg Gln Gln Thr
405 410 415

Gly Ile

<210> 83

<211> 418

<212> PRT

<213> Homo sapiens

<400> 83

Met Tyr Arg Pro Ala Arg Val Thr Ser Thr Ser Arg Phe Leu Asn Pro
1 5 10 15

Tyr Val Val Cys Phe Ile Val Val Ala Gly Val Val Ile Leu Ala Val
20 25 30

Thr Ile Ala Leu Leu Val Tyr Phe Leu Ala Phe Asp Gln Lys Ser Tyr
35 40 45

Phe Tyr Arg Ser Ser Phe Gln Leu Leu Asn Val Glu Tyr Asn Ser Gln
50 55 60

Leu Asn Ser Pro Ala Thr Gln Glu Tyr Arg Thr Leu Ser Gly Arg Ile
65 70 75 80

Glu Ser Leu Ile Thr Lys Thr Phe Lys Glu Ser Asn Leu Arg Asn Gln
85 90 95

Phe Ile Arg Ala His Val Ala Lys Leu Arg Gln Asp Gly Ser Gly Val
100 105 110

Arg Ala Asp Val Val Met Lys Phe Gln Phe Thr Arg Asn Asn Asn Gly
115 120 125

Ala Ser Met Lys Ser Arg Ile Glu Ser Val Leu Arg Gln Met Leu Asn
130 135 140

Asn Ser Gly Asn Leu Glu Ile Asn Pro Ser Thr Glu Ile Thr Ser Leu
145 150 155 160

Thr Asp Gln Ala Ala Ala Asn Trp Leu Ile Asn Glu Cys Gly Ala Gly
165 170 175

Pro Asp Leu Ile Thr Leu Ser Glu Gln Arg Ile Leu Gly Gly Thr Glu
180 185 190

Ala Glu Glu Gly Ser Trp Pro Trp Gln Val Ser Leu Arg Leu Asn Asn
195 200 205

Ala His His Cys Gly Gly Ser Leu Ile Asn Asn Met Trp Ile Leu Thr
210 215 220

Ala Ala His Cys Phe Arg Ser Asn Ser Asn Pro Arg Asp Trp Ile Ala
225 230 235 240

Thr Ser Gly Ile Ser Thr Thr Phe Pro Lys Leu Arg Met Arg Val Arg
245 250 255

Asn Ile Leu Ile His Asn Asn Tyr Lys Ser Ala Thr His Glu Asn Asp
260 265 270

Ile Ala Leu Val Arg Leu Glu Asn Ser Val Thr Phe Thr Lys Asp Ile
275 280 285

His Ser Val Cys Leu Pro Ala Ala Thr Gln Asn Ile Pro Pro Gly Ser
290 295 300

Thr Ala Tyr Val Thr Gly Trp Gly Ala Gln Glu Tyr Ala Gly His Thr
305 310 315 320

Val Pro Glu Leu Arg Gln Gly Gln Val Arg Ile Ile Ser Asn Asp Val
325 330 335

Cys Asn Ala Pro His Ser Tyr Asn Gly Ala Ile Leu Ser Gly Met Leu
340 345 350

Cys Ala Gly Val Pro Gln Gly Gly Val Asp Ala Cys Gln Gly Asp Ser
355 360 365

Gly Gly Pro Leu Val Gln Glu Asp Ser Arg Arg Leu Trp Phe Ile Val
370 375 380

Gly Ile Val Ser Trp Gly Asp Gln Cys Gly Leu Pro Asp Lys Pro Gly
385 390 395 400

Val Tyr Thr Arg Val Thr Ala Tyr Leu Asp Trp Ile Arg Gln Gln Thr
405 410 415

Gly Ile

<210> 84

<211> 489

<212> DNA

<213> Homo sapiens

<400> 84

```

aaaagggttaa gcttgatgat taccaggaac gaatgaacaa aggggaaagg cttaatcaag 60
atcagctgga tgcggtttct aagtaccagg aagtcacaaa taatttggag tttgcaaaag 120
aattacagag gagtttcatg gcactaagtc aagatattca gaaaacaata aagaagacag 180
cacgtcggga gcagcttatg agagaagaag ctgaacagaa acgtttaaaa actgtacttg 240
agctacagta tgttttggac aaattgggag atgatgaagt gcggactgac ctgaaacaag 300
gtttgaatgg agtgccaata ttgtccgaag aggagttgtc attgttggat gaattctata 360
agctagtaga ccctgaacgg gacatgagct tgagggttga tgaacagtat gaacatgcct 420
ccattcacct gtgggacctg ctggaaggga aggaaaaacc tgtatgtgga accacctata 480
aagttctaa

```

<210> 85

<211> 304

<212> DNA

<213> Homo sapiens

<400> 85

```

gggacctgga ggaggccacg ctgcagcatg aagccacagc agccaccctg aggaagaagc 60
acgcggacag cgtggccgag ctgggggagc agatcgacaa cctgcagcgg gtgaagcaga 120
agctggagaa ggagaagagc gagatgaaga tggagatcga tgacctcgtc tgtaacatgg 180
aggatcatctc caaatctaag ggaaaccttg agaagatgtg ccgcacactg gaggaccaag 240
tgagtgaact gaagaccacg gaggaggaac agcagcggct gatcaatgaa ctgactgcgc 300
agag

```

<210> 86

<211> 296

<212> DNA

<213> Homo sapiens

<400> 86

```

gaaaatcctt- cctttgaatg ggaatctcca agcagttgaa ttgggcgaaa aaagaacctc 60
ttccttaagg attaaaatgt ttagggcaac acgtgttact tccacttcca gatttctgaa 120
tccatatgtt gtatgtttcc ttgtcctccc aggggttgtg atcctggcag tccccatagc 180
tctacttggt tacttttttag cttttgatca aaaatcttac ttttattgga gcaattttcc 240
actcccaaat gttgaatata atagtccgtt taattccccc gcttcaccgg gaattc 296

```

<210> 87

<211> 904

<212> DNA

<213> Homo sapiens

<400> 87

```

gtgtccagga aacgattcat gaacataaca agcttgctgc aaattcagat catctcatgc 60
agattcaaaa atgtgagttg gtcttgatcc acacctacc agttgggtgaa gacagccttg 120
tatctgatcg ttctaaaaaa gagttgtccc cggttttaac cagtgaagtt catagtgttc 180
gtgcaggacg gcatcttgct accaaattga atattttagt acagcaacat tttgacttgg 240
cttcaactac tattacaaat attccaatga aggaagaaca gcatgctaac acatctgcca 300
attatgatgt ggagctactt catcacaag atgcacatgt agatttcctg aaaagtgggtg 360

```

```

attcgcatct aggtggcggc agtcgagaag gctcgtttta agaaacaata acattaaagt 420
ggtgtacacc aaggacaaat aacattgaat tacactattg tactggagct tatcggattt 480
cacctgtaga tgtaaatagt agaccttcct cctgccttac taattttctt ctaaatgggc 540
gttctgtttt attggaacaa ccacgaaagt caggttctaa agtcattagt catatgctta 600
gtagccatgg aggagagatt tttttgcacg tccttagcag ttctcgatcc attctagaag 660
atccaccttc aattagtga g gatgtggag gaagagttac agactaccgg attacagatt 720
ttggtgaatt tatgagggga aaacagatta actccttttc tacaccccag atataaaatc 780
gatggaagtc ttgaggtccc ttggaaccg agccaaaaga tcagttaaaa aaacataccc 840
gttactggcc tatgatttca aaaaccacc atttttaaca tgcaagcggg agttccgtta 900
acca
904

```

<210> 88

<211> 387

<212> DNA

<213> Homo sapiens

<400> 88

```

cgtctctccc ccagtttgcc gttcaccccg agcgctcggg acttgccgat agtgggtgacg 60
gcggaacat gtctgtggct ttgcgcccc cgaggcagcg aggcaagggg gagatcactc 120
ccgctgcgat tcagaagatg ttggatgaca ataaccatct tattcagtg ataattggact 180
ctcagaataa aggaaagacc tcagagtgtt cttagtatca gcagatgttg cacacaaact 240
tggtatacct tgctacaata gcagattcta atcaaaatat gcagtctctt ttaccagcac 300
caccacaca gaatatgcct atgggtcctg gagggatgaa tcagagcggg cctccccac 360
ctccacgctc tcacaacatg ccttcaa
387

```

<210> 89

<211> 481

<212> DNA

<213> Homo sapiens

<400> 89

```

tgttcttggg cctgcggtgc tatagagcag gctcttctag gttggcagtt gccatggaat 60
ctggacccaa aatgttgccc cccgtttgccc tgggtggaaaa taacaatgag cagctatttg 120
tgaaccagca agctatacag attcttgaaa agatttctca gccagtgggtg gtgggtggcca 180
ttgtaggact gtaccgtaca gggaaatcct acttgatgaa ccatctggca ggacagaatc 240
atggcttccc tctgggtccc acggtgcagt ctgaaaccaa gggcatctgg atgtggtgag 300
tgccccaccc atccaagcca aaccacaccc tggctcttct ggacaccgaa ggtctgggcg 360
atgtggaaaa ggttgaccct aagaatgact cctggatctt tgccctgggt gtgctcctgt 420
gcagcacctt tgtctacaac agcatgagca ccatcaacca ccaggccctg gagcagctgc 480
a
481

```

<210> 90

<211> 491

<212> DNA

<213> Homo sapiens

<400> 90

```

tgaaaaactgt tcttggaact gcggtgctat agagcagggt ggcagttgcc atggaatctg 60
gacccaaaat gttggcccc gtttgccctgg tggaaaaata caatgagcag ctattggtga 120
accagcaagc tatacagatt cttgaaaaga ttcttcagcc agtgggtgggtg gtggccattg 180
taggactgta ccgtacaggg aaatcctact tgatgaacca tctggcagga cagaatcatg 240
gttccctctt gggctccacg gtgcagtcct aaaccaaggg catctggatg tgggtgcgtgc 300
cccacccatc caagccaaac cacacctgg tccttctgga caccgaagggt ctgggcgatg 360
tggaaaagggt tgaccctaag aatgactcct ggatctttgc cctggctgtg ctctgtgca 420
gcacctttgt ctacaacagc atgagcacca tcaaccacca agccctggag cagctgcatt 480

```

atgtgacgga c

491

<210> 91

<211> 488

<212> DNA

<213> Homo sapiens

<400> 91

```

ttcgacagtc agccgcatct tcttttgcgt cgccagccga gccacatcgc tcagacacca 60
tggggaaggt gaaggtcggg gtcaacggat ttggctgcat tgggcgcctg gtcaccagg 120
ctgcttttaa ctctggtaaa gtggatattg ttgccatcaa tgaccccttc attgacctca 180
actacatggt ttacatgttc caatatgatt ccacccatgg caaattccat ggcaccgtcg 240
aggctgagaa cgggaagctt gtcacatg gaaatcccat caccatcttc caggagcgag 300
atccctccaa aatcaagtgg ggcgatgctg gcgctgagta cgctgtggag tccactggcg 360
tcttcacca catggagaag gctggggctc atttgcagg gggagccaaa agggtcacat 420
tctctgcccc tctgtgatg ccccatgttc gtcattgggtg tgaacatga gaagtatgac 480
acagcctc

```

488

<210> 92

<211> 384

<212> DNA

<213> Homo sapiens

<400> 92

```

gacagtcagc cgcattctct tttgcgtcgc cagccgagcc acatcgctca gacaccatgg 60
ggaaggtgaa ggtcggagtc aacggatttg gtcgtattgg gcgcctgggc accagggtcg 120
cttttaactc tggtaaaagt gatattgttg ccatcaatga ccccttcatt gacctcaact 180
acatggttta catgttccaa tatgattcca cccatggcaa attccatggc accgtcgagg 240
ctgagaacgg gaagcttgtc atcaatggaa atcccatcac catcttccag gagcgagatc 300
cctccaaaat caagtggggc gatactggcg ctgagtacgt cgtggagtcc actggcgctc 360
tcaccaccat ggagaaggct gggg

```

384

<210> 93

<211> 162

<212> PRT

<213> Homo sapiens

<400> 93

```

Lys Gly Lys Leu Asp Asp Tyr Gln Glu Arg Met Asn Lys Gly Glu Arg
 1           5           10           15
Leu Asn Gln Asp Gln Leu Asp Ala Val Ser Lys Tyr Gln Glu Val Thr
          20           25           30
Asn Asn Leu Glu Phe Ala Lys Glu Leu Gln Arg Ser Phe Met Ala Leu
          35           40           45
Ser Gln Asp Ile Gln Lys Thr Ile Lys Lys Thr Ala Arg Arg Glu Gln
          50           55           60
Leu Met Arg Glu Glu Ala Glu Gln Lys Arg Leu Lys Thr Val Leu Glu
          65           70           75           80
Leu Gln Tyr Val Leu Asp Lys Leu Gly Asp Asp Glu Val Arg Thr Asp
          85           90           95

```

Leu Lys Gln Gly Leu Asn Gly Val Pro Ile Leu Ser Glu Glu Glu Leu
 100 105 110

Ser Leu Leu Asp Glu Phe Tyr Lys Leu Val Asp Pro Glu Arg Asp Met
 115 120 125

Ser Leu Arg Leu Asn Glu Gln Tyr Glu His Ala Ser Ile His Leu Trp
 130 135 140

Asp Leu Leu Glu Gly Lys Glu Lys Pro Val Cys Gly Thr Thr Tyr Lys
 145 150 155 160

Val Leu

<210> 94

<211> 100

<212> PRT

<213> Homo sapiens

<400> 94

Asp Leu Glu Glu Ala Thr Leu Gln His Glu Ala Thr Ala Ala Thr Leu
 1 5 10 15

Arg Lys Lys His Ala Asp Ser Val Ala Glu Leu Gly Glu Gln Ile Asp
 20 25 30

Asn Leu Gln Arg Val Lys Gln Lys Leu Glu Lys Glu Lys Ser Glu Met
 35 40 45

Lys Met Glu Ile Asp Asp Leu Ala Cys Asn Met Glu Val Ile Ser Lys
 50 55 60

Ser Lys Gly Asn Leu Glu Lys Met Cys Arg Thr Leu Glu Asp Gln Val
 65 70 75 80

Ser Glu Leu Lys Thr Gln Glu Glu Glu Gln Gln Arg Leu Ile Asn Glu
 85 90 95

Leu Thr Ala Gln
 100

<210> 95

<211> 99

<212> PRT

<213> Homo sapiens

<400> 95

Lys Ile Leu Pro Leu Asn Gly Asn Leu Gln Ala Val Glu Leu Gly Glu
 1 5 10 15

Lys Arg Thr Ser Ser Leu Arg Ile Lys Met Phe Arg Ala Thr Arg Val
 20 25 30

Thr Ser Thr Ser Arg Phe Leu Asn Pro Tyr Val Val Cys Phe Leu Val
 35 40 45
 Leu Pro Gly Val Val Ile Leu Ala Val Pro Ile Ala Leu Leu Val Tyr
 50 55 60
 Phe Leu Ala Phe Asp Gln Lys Ser Tyr Phe Tyr Trp Ser Asn Phe Pro
 65 70 75 80
 Leu Pro Asn Val Glu Tyr Asn Ser Pro Phe Asn Ser Pro Ala Ser Pro
 85 90 95
 Gly Ile Pro

<210> 96
 <211> 257
 <212> PRT
 <213> Homo sapiens

<400> 96
 Val Gln Glu Thr Ile His Glu His Asn Lys Leu Ala Ala Asn Ser Asp
 1 5 10 15
 His Leu Met Gln Ile Gln Lys Cys Glu Leu Val Leu Ile His Thr Tyr
 20 25 30
 Pro Val Gly Glu Asp Ser Leu Val Ser Asp Arg Ser Lys Lys Glu Leu
 35 40 45
 Ser Pro Val Leu Thr Ser Glu Val His Ser Val Arg Ala Gly Arg His
 50 55 60
 Leu Ala Thr Lys Leu Asn Ile Leu Val Gln Gln His Phe Asp Leu Ala
 65 70 75 80
 Ser Thr Thr Ile Thr Asn Ile Pro Met Lys Glu Glu Gln His Ala Asn
 85 90 95
 Thr Ser Ala Asn Tyr Asp Val Glu Leu Leu His His Lys Asp Ala His
 100 105 110
 Val Asp Phe Leu Lys Ser Gly Asp Ser His Leu Gly Gly Gly Ser Arg
 115 120 125
 Glu Gly Ser Phe Lys Glu Thr Ile Thr Leu Lys Trp Cys Thr Pro Arg
 130 135 140
 Thr Asn Asn Ile Glu Leu His Tyr Cys Thr Gly Ala Tyr Arg Ile Ser
 145 150 155 160
 Pro Val Asp Val Asn Ser Arg Pro Ser Ser Cys Leu Thr Asn Phe Leu
 165 170 175

Leu Asn Gly Arg Ser Val Leu Leu Glu Gln Pro Arg Lys Ser Gly Ser
 180 185 190
 Lys Val Ile Ser His Met Leu Ser Ser His Gly Gly Glu Ile Phe Leu
 195 200 205
 His Val Leu Ser Ser Ser Arg Ser Ile Leu Glu Asp Pro Pro Ser Ile
 210 215 220
 Ser Glu Gly Cys Gly Gly Arg Val Thr Asp Tyr Arg Ile Thr Asp Phe
 225 230 235 240
 Gly Glu Phe Met Arg Gly Lys Gln Ile Asn Ser Phe Ser Thr Pro Gln
 245 250 255
 Ile

<210> 97
 <211> 128
 <212> PRT
 <213> Homo sapiens

<400> 97
 Ser Leu Pro Gln Phe Ala Val His Pro Glu Arg Ser Gly Leu Ala Asp
 1 5 10 15
 Ser Gly Asp Gly Gly Asn Met Ser Val Ala Phe Ala Ala Pro Arg Gln
 20 25 30
 Arg Gly Lys Gly Glu Ile Thr Pro Ala Ala Ile Gln Lys Met Leu Asp
 35 40 45
 Asp Asn Asn His Leu Ile Gln Cys Ile Met Asp Ser Gln Asn Lys Gly
 50 55 60
 Lys Thr Ser Glu Cys Ser Gln Tyr Gln Gln Met Leu His Thr Asn Leu
 65 70 75 80
 Val Tyr Leu Ala Thr Ile Ala Asp Ser Asn Gln Asn Met Gln Ser Leu
 85 90 95
 Leu Pro Ala Pro Pro Thr Gln Asn Met Pro Met Gly Pro Gly Gly Met
 100 105 110
 Asn Gln Ser Gly Pro Pro Pro Pro Pro Arg Ser His Asn Met Pro Ser
 115 120 125

<210> 98
 <211> 159
 <212> PRT
 <213> Homo sapiens

<400> 98

Phe Leu Asp Leu Arg Cys Tyr Arg Ala Gly Ser Ser Arg Leu Ala Val
 1 5 10 15
 Ala Met Glu Ser Gly Pro Lys Met Leu Ala Pro Val Cys Leu Val Glu
 20 25 30
 Asn Asn Asn Glu Gln Leu Leu Val Asn Gln Gln Ala Ile Gln Ile Leu
 35 40 45
 Glu Lys Ile Ser Gln Pro Val Val Val Ala Ile Val Gly Leu Tyr
 50 55 60
 Arg Thr Gly Lys Ser Tyr Leu Met Asn His Leu Ala Gly Gln Asn His
 65 70 75 80
 Gly Phe Pro Leu Gly Ser Thr Val Gln Ser Glu Thr Lys Gly Ile Trp
 85 90 95
 Met Trp Cys Val Pro His Pro Ser Lys Pro Asn His Thr Leu Val Leu
 100 105 110
 Leu Asp Thr Glu Gly Leu Gly Asp Val Glu Lys Gly Asp Pro Lys Asn
 115 120 125
 Asp Ser Trp Ile Phe Ala Leu Ala Val Leu Leu Cys Ser Thr Phe Val
 130 135 140
 Tyr Asn Ser Met Ser Thr Ile Asn His Gln Ala Leu Glu Gln Leu
 145 150 155

<210> 99

<211> 147

<212> PRT

<213> Homo sapiens

<400> 99

Met Glu Ser Gly Pro Lys Met Leu Ala Pro Val Cys Leu Val Glu Asn
 1 5 10 15
 Asn Asn Glu Gln Leu Leu Val Asn Gln Gln Ala Ile Gln Ile Leu Glu
 20 25 30
 Lys Ile Ser Gln Pro Val Val Val Val Ala Ile Val Gly Leu Tyr Arg
 35 40 45
 Thr Gly Lys Ser Tyr Leu Met Asn His Leu Ala Gly Gln Asn His Gly
 50 55 60
 Phe Pro Leu Gly Ser Thr Val Gln Ser Glu Thr Lys Gly Ile Trp Met
 65 70 75 80
 Trp Cys Val Pro His Pro Ser Lys Pro Asn His Thr Leu Val Leu Leu

57

85 90 95
 Asp Thr Glu Gly Leu Gly Asp Val Glu Lys Gly Asp Pro Lys Asn Asp
 100 105 110
 Ser Trp Ile Phe Ala Leu Ala Val Leu Leu Cys Ser Thr Phe Val Tyr
 115 120 125
 Asn Ser Met Ser Thr Ile Asn His Gln Ala Leu Glu Gln Leu His Tyr
 130 135 140
 Val Thr Asp
 145

 <210> 100
 <211> 124
 <212> PRT
 <213> Homo sapiens

 <400> 100
 Met Gly Lys Val Lys Val Gly Val Asn Gly Phe Gly Arg Ile Gly Arg
 1 5 10 15
 Leu Val Thr Arg Ala Ala Phe Asn Ser Gly Lys Val Asp Ile Val Ala
 20 25 30
 Ile Asn Asp Pro Phe Ile Asp Leu Asn Tyr Met Val Tyr Met Phe Gln
 35 40 45
 Tyr Asp Ser Thr His Gly Lys Phe His Gly Thr Val Glu Ala Glu Asn
 50 55 60
 Gly Lys Leu Val Ile Asn Gly Asn Pro Ile Thr Ile Phe Gln Glu Arg
 65 70 75 80
 Asp Pro Ser Lys Ile Lys Trp Gly Asp Ala Gly Ala Glu Tyr Val Val
 85 90 95
 Glu Ser Thr Gly Val Phe Thr Thr Met Glu Lys Ala Gly Ala His Leu
 100 105 110
 Gln Gly Gly Ala Lys Arg Val Ile Ile Ser Ala Pro
 115 120

<210> 101
 <211> 127
 <212> PRT
 <213> Homo sapiens

<400> 101
 Gln Ser Ala Ala Ser Ser Phe Ala Ser Pro Ala Glu Pro His Arg Ser
 1 5 10 15

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<210> 102
<211> 1225
<212> DNA
<213> Homo sapiens
```

```
<210> 103
<211> 741
<212> DNA
<213> Homo sapiens
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<400> 103

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agaaacctca atcggattca gcaaaggaat ggtgttatta tcactacata ccaaagtgtta 60
atcaataact ggcagcaact ttcaagcttt aggggccaag agtttgtgtg ggactatgtc 120
atcctcgtatg aagcacataa aataaaaacc tcactacta agtcagcaat atgtgtcgt 180
gctattcctg caagtaatcg cctcctcctc acaggaaccc caatccagaa taatttacia 240
gaactatggt ccctatttga ttttgcttgt caagggtccc tgctgggaac attaaaaact 300
tttaagatgg agtatgaaaa tcctattact agagcaagag agaaggatgc taccacagga 360
gaaaaagcct tgggatttaa aatatctgaa aacttaatgg caatcataaa accctatttt 420
ctcaggagga ctaaagaaga cgtacagaag aaaaagtcaa gcaaccagaa ggccagactt 480
aatgaaaaga atccagatgt tgatgccatt tgtgaaatgc cttccctttc caggagaaat 540
gatttaatta tttggatacg acttgtgcct ttacaagaag aaatatacag gaaatttgtg 600
tcttttagatc atatcaagga gttgctaag gagacgcgt cacccttggc tgagctaggt 660
gtcttaaga agctgtgtga tcaccttagg ctgctgtctg cacgggcttg ttgtttgcta 720
aatcttggga cattctctgc t 741
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<210> 104

<211> 321

<212> DNA

<213> Homo sapiens

<400> 104

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ttgctctgcg tcaccaaaga caccaaactg ctgtgtctata aaagtcccaa ggaccagcag 60
cctcagatgg aactgccact ccaaggctgt aacattacgt acatcccgaa agacagcaaa 120
aagaagaagc acgagctgaa gattactcag cagggcacgg acccgcttgt tctcgccgtc 180
cagagcaagg aacaggccga gcagtggctg aaggatgatca aagaagccta cagtgggtgt 240
agtggccccg tggattcaga gtgtcctcct ccaccaagct ccccggtgca caaggcagaa 300
ctggagaaga aactgtcttc a 321
```

<210> 105

<211> 389

<212> DNA

<213> Homo sapiens

<400> 105

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cagcactggc cacactataa aattcaggtt cagaaaaaca gggtaagtca cagacagcaa 60
cgcttccagc atttattttc tttgcaccca tgggcaattt gagaaaattt acctttagaa 120
cgaactctgt taaaggatca gacagtacaa tactttttat tcagaagggt tctgcataaa 180
ggtgatagtc ttttgactta atatattatt gtctcctgcc ttgtgtttct ggaatgaatg 240
aaggctcatt tttagaagat aatctgggtt gtatttgtgt cgtcagattg aattttcatt 300
gcacatgcta cttaatgtct ttaccaaata ataacaaagg gaaagaaaac caaatataga 360
tgtataataa ggaaaagctg gcctataga 389
```

<210> 106

<211> 446

<212> DNA

<213> Homo sapiens

<400> 106

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gccacatttg ccctgggtcat agtttaaaaca ccagggtcctg tgtcacatct ttttgggtgcc 60
acaagtatca ctccattgtt cagagagtaa tgtattagtt ctgccaatt cattcttcac 120
ttttatttct tccatttcat tagcatttat atcagctcaa gaagttaagg ttagaaaatt 180
ttccacttca aattttcagt acagaaatgt gctgtgatgt ttgacaagac tatttcatag 240
taagttagtt aatgtttatt ggccctctgt ctctctctgt tcagacctag gaagcctgag 300
gattacttag ttgttctgtc tctgggtcca caggcagaat ttggcccatc caaagactgg 360
ccaagtgcc aaaaaaggcc tgattaggcc ctgaaattca gtgaaattct gcctgaagaa 420
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acctcttatt gaatttgaaa accata

446

<210> 107

<211> 467

<212> DNA

<213> Homo sapiens

<400> 107

ccgccgctgc cgtcgcccttc ctgggattgg agtctcgagc tttcttcggt cgttcgccgg 60
cggttcgcgc ccttctcgc gcctcggggc tgcgaggctg gggaaggggt tggagggggc 120
tggtgatcgc cgcgtttaag ttgcgctcgg ggccggccatg tcggccggcg aggtcgagcg 180
cctagtgtcg gagctgagcg gcgggaccgg aggggatgag gaggaagagt ggctctatgg 240
cgatgaagat gaagttgaaa ggccagaaga agaaaatgcc agtgctaata ctccatctgg 300
aattgaagat gaaactgctg aaaatggtgt accaaaaccg aaagtgactg agaccgaaga 360
tgatagtgat agtgacagcg atgatgatga agatgatgtg catgtcacta taggagacat 420
taaaacggga gcaccacagt atgggagtta tggtagagca cctgtaa 467

<210> 108

<211> 491

<212> DNA

<213> Homo sapiens

<400> 108

gaaagataca acttccccc aa cccaaaccgg tttgtggagg acgacatgga taagaatgaa 60
atcgccctcg ttgcgtaccg ttaccgcagg tggaaagctg gagatgatat tgaccttatt 120
gtccgttgtg agcacgatgg cgtcatgact ggagccaacg gggaagtgtc cttcatcaac 180
atcaagacac tcaatgagt ggattccagg cactgtaatg gcgttgactg gcgtcagaag 240
ctggactctc agcgaggggc tgcattgcc acggagctga agaacaacag ctacaagttg 300
gcccgggtgga cctgctgtgc ttgctggct ggatctgagt acctcaagct tggttatgtg 360
tctcgggtacc acgtgaaaga ctctcagc cactcatcc taggcaccca gcagttcaag 420
cctaattgagt ttgccagcca gatcaacctg agcgtggaga atgcctgagg cattttacgc 480
tgcgtcattg a 491

<210> 109

<211> 489

<212> DNA

<213> Homo sapiens

<400> 109

ctcagatagt actgaacctt ttatcaacta tgttttttca gtctgacaac caaggcggct 60
actaagtgac taaggggagc gtagtatata gtgtggataa gcaggacaaa ggggtgattc 120
acatcccagg caggacagag caggagatca tgagatttca tcaactcagga tggcttgtga 180
tttattttat tttattcttt ttttttttgg agatggagtc tcaactcttg ccaggctgga 240
gtgcagtggg gcgactcttg ctcaactgcaa cctctgcctc ctgggttcaa gcagttctcc 300
tgcctcagcc tccaagtag ctgggattac aggcgtccgc caccatgccc agccaatttt 360
tgtactttta gtagagatgg ggtttcacca tgttggccag gctgggtctg aactcctgac 420
ctcaggtgat ccaactgcct cggcctccca aagtgtctgg attataggca tgcgccacca 480
tgcccgggc 489

<210> 110

<211> 391

<212> DNA

<213> Homo sapiens

<400> 110

gcggagtcgc ctggctgacc cgagcgctgg tctccgccgg gaaccctggg gcatggagag 60
 gtctgagtac ctcgccgcgc gcgcacgctg catcgccggag ccaggctgcc gctgtcccag 120
 tggagttcca ggagcaccac ctgagtgagg tgcagaatat ggcatctgag gagaagctgg 180
 agcaggtgct gagttccatg aaggagaaca aagtggccat cattggaaag attcataccc 240
 cgatggagta taagggggag ctagcctcct atgatatgcg gctgaggcgt aagttggact 300
 tatttgccaa cgtaatccat gtgaagtcac ttcctgggta tatgactcgg cacaacaatc 360
 tagacctggg gatcattcga gagcagacag a 391

<210> 111

<211> 172

<212> PRT

<213> Homo sapiens

<400> 111

Met Met Lys Leu Lys Ser Asn Gln Thr Arg Thr Tyr Asp Gly Asp Gly
 1 5 10 15

Tyr Lys Lys Arg Ala Ala Cys Leu Cys Phe Arg Ser Glu Ser Glu Glu
 20 25 30

Glu Val Leu Leu Val Ser Ser Ser Arg His Pro Asp Arg Trp Ile Val
 35 40 45

Pro Gly Gly Gly Met Glu Pro Glu Glu Glu Pro Ser Val Ala Ala Val
 50 55 60

Arg Glu Val Cys Glu Glu Ala Gly Val Lys Gly Thr Leu Gly Arg Leu
 65 70 75 80

Val Gly Ile Phe Glu Asn Gln Glu Arg Lys His Arg Thr Tyr Val Tyr
 85 90 95

Val Leu Ile Val Thr Glu Val Leu Glu Asp Trp Glu Asp Ser Val Asn
 100 105 110

Ile Gly Arg Lys Arg Glu Trp Phe Lys Ile Glu Asp Ala Ile Lys Val
 115 120 125

Leu Gln Tyr His Lys Pro Val Gln Ala Ser Tyr Phe Glu Thr Leu Arg
 130 135 140

Gln Gly Tyr Ser Ala Asn Asn Gly Thr Pro Val Val Ala Thr Thr Tyr
 145 150 155 160

Ser Val Ser Ala Gln Ser Ser Met Ser Gly Ile Arg
 165 170

<210> 112

<211> 247

<212> PRT

<213> Homo sapiens

<400> 112

Arg Asn Leu Asn Arg Ile Gln Gln Arg Asn Gly Val Ile Ile Thr Thr

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<210> 113
<211> 107
<212> PRT
<213> Homo sapiens
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<400> 113
Leu Leu Cys Val Ile Lys Asp Thr Lys Leu Leu Cys Tyr Lys Ser Ser

1 5 10 15
 Lys Asp Gln Gln Pro Gln Met Glu Leu Pro Leu Gln Gly Cys Asn Ile
 20 25 30
 Thr Tyr Ile Pro Lys Asp Ser Lys Lys Lys Lys His Glu Leu Lys Ile
 35 40 45
 Thr Gln Gln Gly Thr Asp Pro Leu Val Leu Ala Val Gln Ser Lys Glu
 50 55 60
 Gln Ala Glu Gln Trp Leu Lys Val Ile Lys Glu Ala Tyr Ser Gly Cys
 65 70 75 80
 Ser Gly Pro Val Asp Ser Glu Cys Pro Pro Pro Pro Ser Ser Pro Val
 85 90 95
 His Lys Ala Glu Leu Glu Lys Lys Leu Ser Ser <
 100 105

 <210> 114
 <211> 155
 <212> PRT
 <213> Homo sapiens

 <400> 114
 Glu Arg Tyr Asn Phe Pro Asn Pro Asn Pro Phe Val Glu Asp Asp Met
 1 5 10 15
 Asp Lys Asn Glu Ile Ala Ser Val Ala Tyr Arg Tyr Arg Arg Trp Lys
 20 25 30
 Leu Gly Asp Asp Ile Asp Leu Ile Val Arg Cys Glu His Asp Gly Val
 35 40 45
 Met Thr Gly Ala Asn Gly Glu Val Ser Phe Ile Asn Ile Lys Thr Leu
 50 55 60
 Asn Glu Trp Asp Ser Arg His Cys Asn Gly Val Asp Trp Arg Gln Lys
 65 70 75 80
 Leu Asp Ser Gln Arg Gly Ala Val Ile Ala Thr Glu Leu Lys Asn Asn
 85 90 95
 Ser Tyr Lys Leu Ala Arg Trp Thr Cys Cys Ala Leu Leu Ala Gly Ser
 100 105 110
 Glu Tyr Leu Lys Leu Gly Tyr Val Ser Arg Tyr His Val Lys Asp Ser
 115 120 125
 Ser Arg His Val Ile Leu Gly Thr Gln Gln Phe Lys Pro Asn Glu Phe
 130 135 140
 Ala Ser Gln Ile Asn Leu Ser Val Glu Asn Ala

145

150

155

<210> 115

<211> 129

<212> PRT

<213> Homo sapiens

<400> 115

Gly Val Arg Trp Leu Thr Arg Ala Leu Val Ser Ala Gly Asn Pro Gly
 1 5 10 15

Ala Trp Arg Gly Leu Ser Thr Ser Ala Ala Ala His Ala Ala Ser Arg
 20 25 30

Ser Gln Ala Ala Ala Val Pro Val Glu Phe Gln Glu His His Leu Ser
 35 40 45

Glu Val Gln Asn Met Ala Ser Glu Glu Lys Leu Glu Gln Val Leu Ser
 50 55 60

Ser Met Lys Glu Asn Lys Val Ala Ile Ile Gly Lys Ile His Thr Pro
 65 70 75 80

Met Glu Tyr Lys Gly Glu Leu Ala Ser Tyr Asp Met Arg Leu Arg Arg
 85 90 95

Lys Leu Asp Leu Phe Ala Asn Val Ile His Val Lys Ser Leu Pro Gly
 100 105 110

Tyr Met Thr Arg His Asn Asn Leu Asp Leu Val Ile Ile Arg Glu Gln
 115 120 125

Thr

<210> 116

<211> 550

<212> DNA

<213> Homo sapiens

<400> 116

gaattcggca ccagcctcag agccccccag cccggctacc accccttgcg gaaaggtacc 60
 catctgcatt cctgcccgtc gggacctggt ggacagtgca gcctccttgg cctctagcct 120
 tggctcaccg ctgcctagag ccaaggagct catcctgaat gaccttcccg ccagcactcc 180
 tgctccaaa tcctgtgact cctccccgcc ccaggacgct tccaccccca ggcccagetc 240
 ggccagtcac ctctgccagc ttgctgcaa gccagcacct tccacggaca gcgtcgccct 300
 gaggagcccc ctgactctgt ccagtcctt caccacgtcc ttcagcctgg gctcccacag 360
 cactctcaac ggagacctct ccgtgcccag ctctacgtc agcctccacc tgtcccccca 420
 ggtcagcagc tctgtggtgt acggacgttc ccccgatgag gcatttgagt ctcatcccca 480
 tctccgaggg tcattcgtct cttcctccct acccagcatc cctgggggaa agccggccta 540
 ctccttccac 550

<210> 117

<211> 154

<212> DNA

<213> Homo sapiens

<400> 117

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ttctgaggga aagccgagtg gagtgggcca cccggcgccg gtgacaatga gttttcttgg 60
aggctttttt ggtcccatct gtgagattga tgttgccctt aatgatgggg aaaccaggaa 120
aatggcagaa atgaaaactg aggatggcaa agta

```

154

<210> 118

<211> 449

<212> DNA

<213> Homo sapiens

<400> 118

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gaattcggca ccaggggccc cagcccagtg gtcgccgcca tggcttcgcc gcagctctgc 60
cgcgcgctgg tgcggcgca atgggtggcg gaggcgctgc gggccccgcg cgctgggcag 120
cctctgcagc tgctggacgc ctctgtgtac ctgccgaagc tggggcgcca cgcgcgacgc 180
gagttcgagg agcggccacat cccggggcgcc gctttcttcg acatcgacca gtgcagcgac 240
cgcacctcgc cctacgacca catgctgccc ggggcccagc atttcgcgga gtacgcaggc 300
cgccctggcg tggggcgcgcc caccacgctc gtgatctacg acgccagcga ccagggcctc 360
tactccgccc cgcgcgtctg gtggatgttc cgcgccttcg gccaccacgc cgtgtcactg 420
cttgatggcg gcttcggcca ctggctgcg

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449

<210> 119

<211> 642

<212> DNA

<213> Homo sapiens

<400> 119

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gaattcggca cgagcagtaa cccgaccgcc gctgggtcttc gctggacacc atgaatcaca 60
ctgtccaaac cttcttctct cctgtcaaca gtggccagcc ccccaactat gagatgctca 120
aggaggagca cgagggtggc gtgctggggg cgccccacaa ccttgctccc ccgacgtcca 180
ccgtgatcca catccgcagc gagacctccg tgcccagcca tgcgtcttgg tccctgttca 240
acacctctt catgaacccc tgcgtgcttg gcttcatagc attcgctac tccgtgaagt 300
ctagggacag gaagatgggt ggcgacgtga ccggggccca ggcctatgcc tccaccgcca 360
agtgcctgaa catctgggccc ctgattctgg gcacctcat gaccattctg ctcatcgcca 420
tcccagtgct gatcttccag gcctatggat agatcaggag gcactactga ggccaggagc 480
tctgcccatt acctgtatcc cactactcc aacttccatt cctcgccctg ccccccggagc 540
cgagtccctg atcagccctt tatectcaca cgcttttcta caatggcatt caataaagtg 600
cacgtgttcc tgggtgaaaa aaaaaaaaaa aaaaaactcg ag

```

642

<210> 120

<211> 603

<212> DNA

<213> Homo sapiens

<400> 120

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gaattcggca cgagccacaa cagccactac gactgcatec actggatcca cggccacccc 60
gtcctccacc ccgggaacag ctccccctcc caaagtgtg accagcccgg ccaccacacc 120
catgtccacc atgtccacaa tctacacctc ctctactcca gagaccaccc acacctccac 180
agtgtgacc accacagcca ccatgacaag ggccaccaat tccacggcca caccctcctc 240
cactctgggg acgaccggga tctcactga gctgaccaca acagccacta caactgcagc 300
cactggatcc acggccaccc tgcctccac cccagggacc acctggatcc tcacagagcc 360
gagcactata gccaccgtga tgggtgccac cggttccacg gccaccgcct cctccactct 420
gggaacagct cacaccccca aagtgggtgac caccatggcc actatgcccc cagccactgc 480

```

ctccacggtt cccagctcgt ccaccgtggg gaccaccgcg acccctgcag tgctccccag 540
 cagcctgccca accttcagcg tgcctactgt gtctctctca gtcttcacca ccttgagacc 600
 cac 603

<210> 121

<211> 178

<212> PRT

<213> Homo sapiens

<400> 121

Ser Glu Pro Pro Ser Pro Ala Thr Thr Pro Cys Gly Lys Val Pro Ile
 1 5 10 15

Cys Ile Pro Ala Arg Arg Asp Leu Val Asp Ser Pro Ala Ser Leu Ala
 20 25 30

Ser Ser Leu Gly Ser Pro Leu Pro Arg Ala Lys Glu Leu Ile Leu Asn
 35 40 45

Asp Leu Pro Ala Ser Thr Pro Ala Ser Lys Ser Cys Asp Ser Ser Pro
 50 55 60

Pro Gln Asp Ala Ser Thr Pro Arg Pro Ser Ser Ala Ser His Leu Cys
 65 70 75 80

Gln Leu Ala Ala Lys Pro Ala Pro Ser Thr Asp Ser Val Ala Leu Arg
 85 90 95

Ser Pro Leu Thr Leu Ser Ser Pro Phe Thr Thr Ser Phe Ser Leu Gly
 100 105 110

Ser His Ser Thr Leu Asn Gly Asp Leu Ser Val Pro Ser Ser Tyr Val
 115 120 125

Ser Leu His Leu Ser Pro Gln Val Ser Ser Ser Val Val Tyr Gly Arg
 130 135 140

Ser Pro Val Met Ala Phe Glu Ser His Pro His Leu Arg Gly Ser Ser
 145 150 155 160

Val Ser Ser Ser Leu Pro Ser Ile Pro Gly Gly Lys Pro Ala Tyr Ser
 165 170 175

Phe His

<210> 122

<211> 36

<212> PRT

<213> Homo sapiens

<400> 122

Met Ser Phe Leu Gly Gly Phe Phe Gly Pro Ile Cys Glu Ile Asp Val
 1 5 10 15

Ala Leu Asn Asp Gly Glu Thr Arg Lys Met Ala Glu Met Lys Thr Glu
 20 25 30

Asp Gly Lys Val
 35

<210> 123
 <211> 136
 <212> PRT
 <213> Homo sapiens

<400> 123
 Met Ala Ser Pro Gln Leu Cys Arg Ala Leu Val Ser Ala Gln Trp Val
 1 5 10 15

Ala Glu Ala Leu Arg Ala Pro Arg Ala Gly Gln Pro Leu Gln Leu Leu
 20 25 30

Asp Ala Ser Trp Tyr Leu Pro Lys Leu Gly Arg Asp Ala Arg Arg Glu
 35 40 45

Phe Glu Glu Arg His Ile Pro Gly Ala Ala Phe Phe Asp Ile Asp Gln
 50 55 60

Cys Ser Asp Arg Thr Ser Pro Tyr Asp His Met Leu Pro Gly Ala Glu
 65 70 75 80

His Phe Ala Glu Tyr Ala Gly Arg Leu Gly Val Gly Ala Ala Thr His
 85 90 95

Val Val Ile Tyr Asp Ala Ser Asp Gln Gly Leu Tyr Ser Ala Pro Arg
 100 105 110

Val Trp Trp Met Phe Arg Ala Phe Gly His His Ala Val Ser Leu Leu
 115 120 125

Asp Gly Gly Leu Arg His Trp Leu
 130 135

<210> 124
 <211> 133
 <212> PRT
 <213> Homo sapiens

<400> 124
 Met Asn His Thr Val Gln Thr Phe Phe Ser Pro Val Asn Ser Gly Gln
 1 5 10 15

Pro Pro Asn Tyr Glu Met Leu Lys Glu Glu His Glu Val Ala Val Leu
 20 25 30

Gly Ala Pro His Asn Pro Ala Pro Pro Thr Ser Thr Val Ile His Ile
 35 40 45

Arg Ser Glu Thr Ser Val Pro Asp His Val Val Trp Ser Leu Phe Asn
50 55 60

Thr Leu Phe Met Asn Pro Cys Cys Leu Gly Phe Ile Ala Phe Ala Tyr
65 70 75 80

Ser Val Lys Ser Arg Asp Arg Lys Met Val Gly Asp Val Thr Gly Ala
85 90 95

Gln Ala Tyr Ala Ser Thr Ala Lys Cys Leu Asn Ile Trp Ala Leu Ile
100 105 110

Leu Gly Ile Leu Met Thr Ile Leu Leu Ile Val Ile Pro Val Leu Ile
115 120 125

Phe Gln Ala Tyr Gly
130

<210> 125

<211> 195

<212> PRT

<213> Homo sapiens

<400> 125

Thr Thr Ala Thr Thr Thr Ala Ser Thr Gly Ser Thr Ala Thr Pro Ser
1 5 10 15

Ser Thr Pro Gly Thr Ala Pro Pro Pro Lys Val Leu Thr Ser Pro Ala
20 25 30

Thr Thr Pro Met Ser Thr Met Ser Thr Ile His Thr Ser Ser Thr Pro
35 40 45

Glu Thr Thr His Thr Ser Thr Val Leu Thr Thr Thr Ala Thr Met Thr
50 55 60

Arg Ala Thr Asn Ser Thr Ala Thr Pro Ser Ser Thr Leu Gly Thr Thr
65 70 75 80

Arg Ile Leu Thr Glu Leu Thr Thr Thr Ala Thr Thr Thr Ala Ala Thr
85 90 95

Gly Ser Thr Ala Thr Leu Ser Ser Thr Pro Gly Thr Thr Trp Ile Leu
100 105 110

Thr Glu Pro Ser Thr Ile Ala Thr Val Met Val Pro Thr Gly Ser Thr
115 120 125

Ala Thr Ala Ser Ser Thr Leu Gly Thr Ala His Thr Pro Lys Val Val
130 135 140

Thr Thr Met Ala Thr Met Pro Thr Ala Thr Ala Ser Thr Val Pro Ser
145 150 155 160

Ser Ser Thr Val Gly Thr Thr Arg Thr Pro Ala Val Leu Pro Ser Ser
 165 170 175

Leu Pro Thr Phe Ser Val Ser Thr Val Ser Ser Ser Val Leu Thr Thr
 180 185 190

Leu Arg Pro
 195

<210> 126
 <211> 509
 <212> DNA
 <213> homo sapien

<400> 126
 gaattcggca cgagccaagt accccctgag gaattctgcag cctgcatctg agtacaccgt 60
 atccctcgtg gccataaagg gcaaccaaga gagccccaaa gccactggag tctttaccac 120
 actgcagcct gggagctcta ttccacctta caacaccgag gtgactgaga ccaccattgt 180
 gatcacatgg acgcctgctc caagaattgg ttttaagctg ggtgtacgac caagccaggg 240
 aggagaggca ccacgagaag tgacttcaga ctcaggaagc atcgttgtgt ccggttgac 300
 tccaggagta gaatacgtct acaccatcca agtccctgaga gatggacagg aaagagatgc 360
 gccaatgtga aacaaagtgg tgacaccatt gtctccacca acaaacttgc atctggaggc 420
 aaaccctgac actggagtgc tcacagtctc ctggagagga gcaccacccc agacattact 480
 gggatatagaa ttaccacaac ccctacaaa 509

<210> 127
 <211> 500
 <212> DNA
 <213> homo sapien

<400> 127
 gaattcggca cgagccactg atgtccgggg agtcagccag gagcttgggg aaggggaagcg 60
 cgccccggg gccggtcccg gagggctcga tccgcatcta cagcatgagg ttctgcccgt 120
 ttgctgagag gacgcgtcta gtccctgaagg ccaagggaat caggcatgaa gtcattcaata 180
 tcaacctgaa aaataagcct gagtgggtct ttaagaaaaa tccctttggg ctgggtgccag 240
 ttctggaaaa cagtcagggg cagctgatct acgagtctgc catcacctgt gagtacctgg 300
 atgaagcata ccaggggaag aagctgttgc cggatgacct ctatgagaaa gcttgccaga 360
 agatgatctt agagttgttt tctaagggtc catccttggg aggaagcttt attagaagcc 420
 aaaataaaga agactatgct ggccataaaag aagaatttcg taaagaattt accaagctag 480
 aggaggttct gactaataag 500

<210> 128
 <211> 500
 <212> DNA
 <213> homo sapien

<400> 128
 agctttcttc tgctgccgct cggtcacgct tgtgcccga gaggaaaca gtgacagacc 60
 tggagactgc agttctctat ccttcacaca gctctttcac catgcctgga tcacttcctt 120
 tgaatgcaga agcttgctgg ccaaaagatg tgggaattgt tgcccttgag atctattttc 180
 cttctcaata tggtgatcaa gcagagttgg aaaaatatga tgggtgtagat gctggaaagt 240
 ataccattgg cttgggccag gccaaagatgg gcttctgcac agatagagaa gatattaact 300
 ctctttgcat gactgtgggt cagaatctta tggagagaaa taacctttcc tatgattgca 360

ttgggcggtt ggaagttgga acagagacaa tcatcgacaa atcaaagtct gtgaagacta 420
 atttgatgca gctgtttgaa gagtctggga atacagatat agaaggaatc gacacaacta 480
 atgcatgcta tggaggcaca 500

<210> 129

<211> 497

<212> DNA

<213> homo sapien

<400> 129

gaattcggca cgagcagagg tctccagagc cttctctctc ctgtgcaaaa tggcaactct 60
 taaggaaaaa ctcattgcac cagttgcgga agaagaggca acagttccaa acaataagat 120
 cactgtagt ggtgttggaac aagttggat ggcgtgtgct atcagcattc tgggaaagtc 180
 tctggctgat gaacttgctc ttgtggatgt ttgggaagat aagcttaaag gagaaatgat 240
 ggatctgcag catgggagct tatttcttca gacacctaaa attgtggcag ataaagatta 300
 ttctgtgacc gccaatctta agattgtagt ggtaactgca ggagtccgct agcaagaagg 360
 ggagagtcgg ctcaatctgg tgcagagaaa tgtaaatgct ttcaaattca ttattcctca 420
 gatcgtcaag tacagtcctg attgcatcat aattgtgggt tccaaccagc tggacattct 480
 tacgtatgtt acctgga 497

<210> 130

<211> 383

<212> DNA

<213> homo sapien

<400> 130

gaattcggca cgagggccgc ggctgccgac tgggtccctt gccgctgtcg ccaccatggc 60
 tccgcaccgc cccgcgcccg cgctgctttg cgcgctgtcc ctggcgctgt gcgcgctgtc 120
 gctgccgctc cgcgcggcca ctgcgtcgcg gggggcgctc caggcggggg cgccccaggg 180
 gcgggtgccc gaggcgcggc ccaacagcat ggtggtggaa caccctgagt tcttcaaggc 240
 agggaaggag cctggcctgc agatctggcg tgtggagaaa gttcgatctg gtggcccgctg 300
 cccaccaacc tttatggaga cttcttcacg ggcgacgcct acgtcatcct gaagacagtg 360
 cagcttaaga acggaaaatc ttg 383

<210> 131

<211> 509

<212> DNA

<213> homo sapien

<400> 131

gaattcggca cgagagtcag ccgcatcttc ttttgcgtcg ccagccgagc cacatcgctc 60
 agacaccatg ggggaaggtga aggtcggagt caacggattt ggctgtattg ggcgccctgt 120
 caccagggtt gcttttaact ctggtaaagt ggatattgtt gccatcaatg accccttcat 180
 tgacctcaac tacatggttt acatgttcca atatgattcc acccatggca aattccatgg 240
 caccgtcaag gctgagaacg ggaagcttgt catcaatgga aatcccatca ccatcttcca 300
 ggagcgagat ccttccaaaa tcaagtggg cgatgctggc gctgagtacg tcgtggagtc 360
 cactggccgt cttcaccacc atggagaagg ctggggctca tttgcagggg ggagccaaaa 420
 gggtcacat ctctgcccc tctgctgacg ccccatgtt cgtcatgggt gtgaaccatg 480
 agaagtatga caacagcctc aagatcatc 509

<210> 132

<211> 357

<212> DNA

<213> homo sapien

<400> 132

gaattcggca	cgagtaagaa	gaagccccta	gaccacagct	ccacaccatg	gactggacct	60
ggaggatcct	cttcttggtg	gcagcagcaa	caggtgccca	ctcccagggtg	caactgggtgc	120
aatctgggtc	tgagttgaag	aagcctgggg	cctcagtgaa	ggtttctctgc	aaggcttctg	180
gacacatctt	cagtatctat	ggtttgaatt	gggtgcgaca	ggccccctggt	caaggccttg	240
agtggatggg	atggatcaaa	gtcgacactg	cgaacccaac	gtatgccag	ggcttcacag	300
gacgatttgt	cttctccctg	gacacctctg	tcagcacggc	atatctgcag	atcagca	357

<210> 133

<211> 468

<212> DNA

<213> homo sapien

<400> 133

gaattcggca	cgaggcgccc	cgaaccgtcc	tcctgctgct	ctcggcgggc	ctggccctga	60
ccgagacctg	ggccggctcc	cactccatga	ggtatttcga	caccgccatg	tcccggccccg	120
gccgcgggga	gccccgcttc	atctcagtg	gctacgtgga	cgacacgcag	ttcgtgaggt	180
tcgacagcga	cgccgcgagt	ccgagagagg	agccgcgggc	gccgtggata	gagcaggagg	240
ggccggagta	ttgggaccgg	aacacacaga	tcttcaagac	caacacaeag	actgaccgag	300
agagcctgcg	gaacctgcgc	ggctactaca	accagagcga	ggccgggtct	cacaccctcc	360
agagcatgta	cggctgcgac	gtggggcccg	acgggcgcct	cctccgcggg	cataaccagt	420
acgcctacga	cggcaaggat	tacatcgccc	tgaacgagga	cctgcgct		468

<210> 134

<211> 214

<212> DNA

<213> homo sapien

<400> 134

gaattcggca	cgagctgcgt	cctgctgagc	tctgttctct	ccagcacctc	ccaaccact	60
agtgcctggg	tctcttgctc	caccaggaac	aagccaccat	gtctcgccag	tcaagtgtgt	120
ccttccggag	cgggggcagt	cgtagcttca	gcaccgctc	tgccatcacc	ccgtctgtct	180
cccgcaccag	cttcacctcc	gtgtccccgt	ccgg			214

<210> 135

<211> 355

<212> DNA

<213> homo sapien

<400> 135

gaattcggca	cgagggtgaac	aggaccggtc	gccatggggc	gtgtgatccg	tggacagagg	60
aagggcgccg	ggtctgtgtt	ccgcgcgcac	gtgaagcacc	gtaaaggcgc	tgcgcgcctg	120
cgcgcctggg	atttcgctga	gcggcacggc	tacatcaagg	gcacgtcaa	ggacatcatc	180
cacgaccggg	gccgcggcgc	gccccctgct	aaggtggtct	tccgggateg	gtatcggttt	240
aagaagcgga	cggagctgtt	cattgccgcc	gagggcatte	acacgggcca	gtttgtgtat	300
tgcggcaaga	aggcccagct	caacattggc	aatgtgctcc	ctgtgggcac	catgc	355

<210> 136

<211> 242

<212> DNA

<213> homo sapien

<400> 136

gaattcggca	cgagccagct	cctaaccgcg	agtgatccgc	cagcctccgc	ctcccagagg	60
gcccggattg	cagacggagt	ctccttcaact	cagtgtctca	tggtgcccag	gctggaggtgc	120

agtgggtgtga tctcgggtcg ctacaacatc cacctcccag cagcctgcct tggcctccca 180
 aagtgccgag attgcagctc tctgcccggc cgccaccctt gtctgggaag tgaggatgct 240
 gt 242

<210> 137

<211> 424

<212> DNA

<213> homo sapien

<400> 137

gaattcggca cgagcccaga tcccagaggtc cgacagcgcc cggcccagat cccacgcct 60
 gccaggagca agccgagagc cagccggccg gcgcactccg actccgagca gtctctgtcc 120
 ttcgaccga gcccgcgccc ctttccggga cccctgcccc gcgggcagcg ctgccaacct 180
 gccggccatg gagaccccggt cccagcggcg cgccaccgcg agcggggcg aggccagctc 240
 cactccgctg tcgcccaccc gcacaccccg gctgcaggag aaggaggacc tgcaggagct 300
 caatgatcgc ttggcggtct acatcgaccg tgtgcgctcg ctggaaacgg agaacgcagg 360
 gctgcgcctt cgcacaccg agtctgaaga ggtggtcagc cgcgaggtgt ccggcatcaa 420
 gcc 424

<210> 138

<211> 448

<212> DNA

<213> homo sapien

<400> 138

gaattcggca cgagcctgtg ttccaggagc cgaatcagaa atgtcatcct caggcacgcc 60
 agacttacct gtcctactca ccgatttgaa gattcaatat actaagatct tcataaacia 120
 tgaatggcat gattcagtga gtggcaagaa atttcctgtc tttaatcctg caactgagga 180
 ggagctctgc caggtagaag aaggagataa ggaggatgtt gacaaggcag tgaaggccgc 240
 aagacaggct ttccagattg gatccccgtg gcgtactatg gatgcttccg agagggggcg 300
 actattatac aagttggctg atttaatcga aagagatcgt ctgctgctgg ccgacaatgg 360
 agtcaatgaa tgggtggaaa ctctattcca atgcatatct gaatgattta gcaggctgca 420
 tcaaaacatt gcgctactgt gcaggttg 448

<210> 139

<211> 510

<212> DNA

<213> homo sapien

<400> 139

gaattcggca cgaggttccg tgcagctcac ggagaagcga atggacaaag tcggcaagta 60
 ccccaaggag ctgcgcaagt gctgcgagga cggcatgcgg gagaaccca tgaggttctc 120
 gtgccagcgc cggaccggtt tcatctccct ggcgaggcgt gcaagaaggc cttcctggac 180
 tgctgcaact acatcacaga gctgcggcgg cagcacgcgc gggccagcca cctggcctgc 240
 caggagtaac ctggatgagg acatcattgc agaagagaac atcgtttccc gaagtgagtt 300
 cccagagagc tggctgtgga acgttgagga cttgaaagag ccaccgaaaa atggaatctc 360
 tacgaagctc atgaatatat ttttgaaaga ctccatcacc acgtgggaga ttctggctgt 420
 gagcatgtcg gacaagaaag ggatctgtgt ggcagacccc ttcgaggtca cagtaatgca 480
 ggacttcttc atcgacctgc ggctacccta 510

<210> 140

<211> 360

<212> DNA

<213> homo sapien

<400> 140

gaattcggca	cgagcggtaa	ctaccccggc	tgcgcacagc	tcggcgctcc	ttcccgctcc	60
ctcacacacc	ggcctcagcc	cgcaccggca	gtagaagatg	gtgaaagaaa	caacttacta	120
cgatgttttg	ggggtcacaa	ccaatgctac	tcaggaagaa	ttgaaaaagg	cttataggaa	180
actggctttg	aagtaccatc	ctgataagaa	cccaaagtaa	ggagagaagt	ttaaacagat	240
ttctcaagct	tacgaagttc	tctctgatgc	aaagaaaagg	gaattatatg	acaaaggagg	300
agaacaggca	attaaagagg	gtggagcagg	tggcggtttt	ggctccccc	tggacatctt	360

<210> 141

<211> 483

<212> DNA

<213> homo sapien

<400> 141

gaattcggca	cgagagcaga	ggctgatctt	tgctggaaaa	cagctggaag	atgggctgca	60
ccctgtctga	ctacaacatc	cagaaagagt	ccaccctgca	cctgggtgctc	cgtctcagag	120
gtgggatgca	aattcttcgtg	aagacactca	ctggcaagac	catcaccctt	gaggtggagc	180
ccagtgcac	catcgagaac	gtcaaaagcaa	agatccagga	caaggaaggc	attcctcctg	240
accagcagag	gttgatcttt	gccggaaaagc	agctggaaga	tgggcgcacc	ctgtctgact	300
acaacatcca	gaaagagtct	accctgcacc	tgggtgctccg	tctcagaggt	gggatgcaga	360
tcttcgtgaa	gaccctgact	ggtaagacca	tcaccctcga	ggtaggagccc	agtgcacacca	420
tcgagaatgt	caaggcaaa	atccaagata	aggaaggcat	tcctcctgat	cagcagaggt	480
tga						483

<210> 142

<211> 500

<212> DNA

<213> homo sapien

<400> 142

gaattcggca	cgaggcggcg	acgaccgccc	ggagcgtgtg	cagcggcggc	ggcgggaagtg	60
gccggcgagc	ccggtccccg	ccggcaccat	gcttcccttg	tcactgctga	agacgggtca	120
gaatcacccc	atgttggtgg	agctgaaaaa	tggggagacg	tacaatggac	actcgggtgag	180
ctgcgacaac	tggatgaaca	ttaacctgct	ccgcggcagc	accatcaagt	acctgcgcct	240
caagttcttg	cggatgccc	agtgtctac	ccgcggcagc	accatcaagt	acctgcgcct	300
ccccgacgag	atcatcgaca	tgggtcaagga	ggaggtggtg	gccaagggcc	gcggcccgcg	360
aggcctgcag	cagcagaagc	agcagaaagg	ccgcggcagc	ggcggcgctg	gccgaggtgt	420
gtttggtggc	cggggccgag	gtgggatccc	gggcacaggc	agaagccagc	cagagaagaa	480
gcctggcaga	caggcgggca					500

<210> 143

<211> 400

<212> DNA

<213> homo sapien

<400> 143

gaattcggca	cgagctcggg	tgtcagcagg	cgtcccaacc	cagcaggaac	tggctcaatt	60
ctcagaagaa	agcgatcggc	cccagggcag	gaaggccggc	tccgggtgcag	ggcgcgccgc	120
ctgcgggctg	cttcgggcca	gggtcgaccc	gagggccagc	gcaagcagcg	gcaacaggag	180
cgcaggagg	acatgaggct	ctgcctgcag	tcagcaactt	ggaatattca	gacttcagac	240
cagcatcaca	gattataacc	ctccgtaaat	catctgcac	ccagctccca	tcaaaagcca	300
gcctgaagga	cccatggaca	cgtgactcca	gtgttctcaa	caacatctta	gatcaagttg	360
gtttgcacaa	catttgcac	tacttgggac	aaagcaagaa			400

<210> 144

<211> 243
 <212> DNA
 <213> homo sapien

<400> 144
 gaattcggca cgagccagct cctaaccgcg agtgatccgc cagcctccgc ctcccagggt 60
 gcccggttg cagacggagt ctcttctact cagtgtctca tgggtgcccag gctggagtgc 120
 agtgggtgtga tctcgggtcg ctacaacatc cacctcccag cagcctgcct tggcctccca 180
 aagtgccgag attgcagcct ctgcccggcc gtcaccccgct ctgggaagtg aggagcgttt 240
 ctg 243

<210> 145
 <211> 450
 <212> DNA
 <213> homo sapien

<400> 145
 gaattcggca cgaggacagc aggaccgtgg aggccgcggc aggggtggca gtgggtggcgg 60
 cggcgggcggc ggcgggtggtg gttacaaccg cagcagtggc ggctatgaac ccagagggtcg 120
 tggaggtggc cgtggaggca gaggtggcat gggcggaagt gaccgtgggtg gcttcaataa 180
 atttgggtggc cctcgggacc aaggatcacg tcatgactcc gaacaggata attcagacaa 240
 caacaccatc tttgtgcaag gcctgggtga gaatgttaca attgagtctg tggctgatta 300
 cttcaagcag attggtatta ttaagacaaa caagaaaacg ggacagccca tgattaattt 360
 gtacacagac agggaaactg gcaagctgaa gggagaggca acggtctctt ttgatgacct 420
 accttcagct aaagcagcct attgactggc 450

<210> 146
 <211> 451
 <212> DNA
 <213> homo sapien

<400> 146
 gaattcggca cgagccatcg agtccctgcc tttegacttg cagagaaatg tctcgtgat 60
 gcgggagatc gacgcgaaat accaagagat cctgaaggag ctacacgagt gctacgagcg 120
 cttcagtcgc gagacagacg gggcgacgaa gcggcggatg ctgcactgtg tgcagcgcg 180
 gctgatccgc accaggagct gggcgacgag aagatccaga tcgtgagcca gatgggtggag 240
 ctggtggaga accgcacgcg gcaggtggac agccacgtgg agctgttcga ggcgcagcag 300
 gagctgggcg acacagcggg caacagcggc aaggctggcg cggacaggcc caaaggcgag 360
 gcggcagcgc aggttgacaa gccaacacagc aagcgtcac ggcggcagcg caacaacgag 420
 aaccgtgaga acgcgtccag caaccacgac c 451

<210> 147
 <211> 400
 <212> DNA
 <213> homo sapien

<400> 147
 gaattcggca cgagctcggg tgtcagcagg cgtcccaacc cagcaggaac tggctcaatt 60
 ctcaagaaga agcgatcggc cccgaggcag gaaggccggc tccggtgcag ggcgcgccgc 120
 ctgcgggctg cttcggggcca gggctgaccc gagggccagc gcaagcagcg gcaacaggag 180
 cgccaggagg acatgaggct ctgcctgcag tcagcaactt ggaatattca gacttcagac 240
 cagcatcaca gattataacc ctccgtaaat catctgcate ccagctccca tcaaaagcca 300
 gcctgaagga cccatggaca cgtgactcca gtgttctcaa caacatctta gatcaagttg 360
 gtttcgacaa catttgcac tacttgggac aaagcaagaa 400

<210> 148
 <211> 503
 <212> DNA
 <213> Homo sapien

<400> 148
 aaaagaattc ggcacgagcg ggcgcgctca tccccctctc ccagcagatt cccactggaa 60
 attcgttgta tgaatcttat tacaagcagg tcgatccggc atacacaggg aggggtggggg 120
 cgagtgaagc tgcgcttttt ctaaagaagt ctggcctctc ggacattatc cttgggaaga 180
 tatgggactt ggcgatcca gaaggtaaag ggttcttgga caaacagggt ttctatgttg 240
 cactgagact ggtggcctgt gcacagagtg gccatgaagt taccttgagc aatctgaatt 300
 tgagcatgcc accgcctaaa tttcacgaca ccagcagccc tctgatgggc acaccgccct 360
 ctgcagaggc cactgggct gtgagggtgg aagaaaaggc caaatttgat gggatttttg 420
 aaagcctctt gccatcaat ggtttgctct ctggagacaa agtcaagcca gtcctcatga 480
 actcaaagct gcctcttgat gtc 503

<210> 149
 <211> 1061
 <212> DNA
 <213> homo sapien

<400> 149
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 gagccctgca gaagctgctg gtcatecttg ccacggagca gccgctcact gcaaagaaga 120
 aggtcctggt tgcactgtgc tccctgctgc gccacttccc ctatgccag cggcagttcc 180
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 gaggacatct tggcagtgct ggcttggcca ttaaattgaa acctgaaggc catcctcttt 780
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 ggcaggaace tgggcccagg agttgcaagt ctctgcttct taccaagcag cagctctgta 960
 ccttgggaag tcgcttaatt gctctgagct tgtttcctca tctgtcagga gtgccattaa 1020
 aggagaaaaa tcacgtaaaa aaaaaaaaaa aaaaactcga g 1061

<210> 150
 <211> 781
 <212> DNA
 <213> homo sapien

<400> 150
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 acccaaaatg gaggaagaga gcggcgcgcc ctgctgcccg agcggcaacg gagctccggg 120
 cccgaagggg gaagaacgac ctactcagaa tgagaagagg aaggagaaaa acataaaaaa 180
 aggaggcaat cgctttgagc catattccaa cccaactaaa agatacagag ccttcattac 240
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 tctgagtggga aggccactga aagtcaagga agatcctgat ggtgaacatg caaggagagc 480

aatgcaaaag gctggaagac ttggaagcac agtattttgta gcaaactctgg attataaaagt	540
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tctggaagat aaagatggga aaagtcgtgg aataggcatt gtgacttttg aacagtcctat	660
tgaagctgtg caagcaatac ctatgtttta tggccagttg ctgtttgata gaccgatgca	720
cgtcaagatg gatgagaggg ctttaccaaa gggagacttt tttcctcctg aacgccacag	780
c	781

<210> 151
 <211> 3275
 <212> DNA
 <213> Homo sapien

<400> 151

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tctgctatcc agtatgttg ctgaccacag gctcaaaactg gaggattata aggatcgctt	180
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gctacataat ttggaatttg ccaaggagct tcaaaaaaac tttctctgggt tgagcctaga	300
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gcacgtacaa aaagacttca aaggggggtt gaatgggtgca gtgtattttgc cttcaaaaga	480
acttgactac ctcatthaagt tttcaaaact gacctgcctt gaaagaaatg aaagtctgag	540
acaaacactt gaaggatcta ctgtctaaat tgctgaactc aggtattttt gaaagtatcc	600
cagttcccaa aaatgccaa gaaaaggaag taccactgga ggaagaaatg ctaatacaat	660
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aatttgccca gccagagata caaccacaag agttctttaa cagacgctat atgcagaag	780
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agtcctttta gtctctgggag gcttctgggt agcaccagga ggtatccaag cctgcagttt	960
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aatccaaagc aggttatgtt caagaggaac aaaagaaaca ggagacacca aagctgtggc	1140
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agccgttaca ggtatttaac gttaatgcac ctctgcctcc acgaaaagaa caagaaataa	1740
aagaatcccc ttattcacct ggctacaatc aaagttttac cacagcaagt acacaaacac	1800
caccccagtg ccaactgccca tctatacatg tagaacaac tgtccattct caagagactg	1860
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ctggacaagg agactcccgt agcatgacct ctgtggatgt gccagtgaca aatccagag	2340
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atggcactta	cgtttttcatt	tttcacatgc	taaagctggc	agtgaatgtg	ccactgtatg	2580
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accatgaaac	tgctagcaat	catgcaattc	ttcagctctt	ccagggagac	cagatatggt	2700
tacgtctgca	caggggagca	atttatggaa	gtagctggaa	atattctacg	ttttcaggct	2760
atcttcttta	tcaagattga	aagtcagtac	agtattgaca	ataaaaaggat	ggtgttctaa	2820
ttagtgggat	tgaaggaaaa	gtagtctttg	ccctcatgac	tgattgggtt	aggaaaatgt	2880
ttttgttcct	agagggagga	ggtccttact	ttttgtttt	ccttcctgag	gtgaaaaatc	2940
aagctgaatg	acaattagca	ctaactctggc	actttataaa	ttgtgatgta	gcctcgctag	3000
tcaagctgtg	aatgtatatt	gtttgcactt	aatccttaac	tgtattaacg	ttcagcttac	3060
taaactgact	gcctcaagtc	caggcaagtt	acaatgcctt	gttgtgcctc	aataaaaaag	3120
ttacatgcaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	3180
aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	3240
aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	tcgag			3275

<210> 152

<211> 2179

<212> DNA

<213> homo sapien

<400> 152

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<212> DNA

<213> Homo sapien

<400> 153

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<211> 1411

<212> DNA

<213> homo sapien

<400> 154

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<211> 678

<212> DNA

<213> homo sapien

<400> 155

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<212> DNA

<213> Homo sapien

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<211> 2313

<212> DNA

<213> homo sapien

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<211> 2114

<212> DNA

<213> homo sapien

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tttttgcaga	aggagcagga	tctgaaaagct	gaaattgaga	agctttgtga	gaagggcaga	840
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aacattatgg	aagagactga	acgggcctgg	aaggcagaga	tcttatcact	agagagccgg	960
aaagagttac	tggtactgaa	actagaagaa	gcagaaaaag	aggcagaatt	gcaccttact	1020
tacctcaagt	caactcccc	aacactggag	acagttcgtt	ccaaacagga	gtgggagacg	1080
agactgaatg	gagttcggat	aatgaaaaag	aatgttcgtg	accaatttaa	tagtcatatc	1140
cagttagtga	ggaacggagc	caagctgagc	agccttcttc	aaatccctac	tcccacttta	1200

cctccacccc	catcagagac	agacttcatg	cttcagggtg	ttcaacccag	tccctctctg	1260
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gatccccgct	ccttgtcttt	cccaatcctg	aaccctgccc	tttcccagcc	cagccagcct	1380
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cctgggtgccg	aattcggcac	gaggtaccac	tggtctgtgt	gctagaggag	ggtgttgcca	1500
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ccggggacgga	ggaggggggtc	accgtgaagc	cactggttgt	gggtgtgggtg	gtgtgtctga	1620
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tggttgtggt	agtcggcact	ttggtagtgt	gagctgttcc	tggggtggaa	gaggggggtgg	1740
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cagtctctgg	agtggaggag	ggtgtggctg	tggacatggt	ggccgtgggt	gtgggtggctc	1860
gtgataggcg	gggtccagggtg	gtgcccaggg	aggaggaggg	gatggctgta	aagctggtag	1920
ctgtgggtgt	gggtggctgtg	cttctcagtg	ctggaagggc	ggttgcagtc	cctggactgg	1980
agaaggaggt	ggctttggag	ctggtgactg	tgggtgtcgt	ggccgtgggtg	ctcacatgtg	2040
gggtgccagc	agttgcctgg	gtggaggagg	cgggtggcctg	ggatccgggtg	ggcaccgtca	2100
cgggagtact	tcta					2114

<210> 159

<211> 278

<212> DNA

<213> homo sapien

<400> 159

gaattcggca	caggtaactt	tgcttggggg	atttataaaaa	aaaaaaaaaa	aaaaaaaaaag	60
tcaaatactt	gagtactaat	ttcctgaaaa	gtatgttccg	atagatgaac	agatcattaa	120
tgcaaatga	gaatcactcc	taaaataggt	aattgtaaaa	attaaattga	caattacctc	180
tctctatgca	gaaggaaata	tcacctatat	gacatcatca	tcattctattg	atatttggctg	240
gcagtgtctaa	taattggtttt	aatgcccaatt	tgtaagaa			278

<210> 160

<211> 848

<212> DNA

<213> homo sapien

<400> 160

gaattcggca	cgagccccag	aggagctcgg	cctgcgctgc	gccacgatgt	ccggggagtc	60
agccaggagc	ttgggggaagg	gaagcgcgcc	cccgggggccc	gtcccggagg	gctegateeg	120
catctacagc	atgagggttc	geccgtttgc	tgagaggacg	cgtctagtcc	tgaaggccaa	180
gggaatcagg	catgaagtca	tcaatatcaa	cctgaaaaat	aagcctgagt	ggttctttta	240
gaaaaatccc	tttgggtctgg	tgccagttct	ggaaaacagt	cagggtcagc	tgatctacga	300
gtctgccatc	acctgtgagt	acctggatga	agcataccca	gggaagaagc	tggtgcccga	360
tgacccctat	gagaaaagctt	gccagaagat	gatcttagag	ttgttttcta	aggtgccatc	420
cttggtagga	agctttatta	gaagccaaaa	taaagaagac	tatgctggcc	taaaagaaga	480
atttcgtaaa	gaatttacca	agctagagga	ggttctgact	aataagaaga	cgaccttctt	540
tggtggcaat	tctatctcta	tgattgatta	cctcatctgg	ccctgggttg	aacggctgga	600
agcaatgaag	ttaaatgagt	gtgtagacca	cactccaaaa	ctgaaactgt	ggatggcagc	660
catgaaggaa	gatcccacag	tctcagccct	gcttactagt	gagaaagact	ggcaagggtt	720
cctagagctc	tacttacaga	acagccctga	ggcctgtgac	tatgggtctc	gaagggggca	780
ggagtgcagc	ataaagctat	gtctgatatt	ttccttcact	aaaaaaaaaa	aaaaaaaaaa	840
aactcgag						848

<210> 161

<211> 432

<212> DNA

<213> homo sapien

<400> 161

gaattcggca	cgagggcaga	ccaagatcct	ggaggaggac	ctggaacaga	tcaagctgtc	60
cttgagagag	cgaggccggg	agctgaccac	tcagaggcag	ctgatgcagg	aacgggcaga	120
ggaagggaag	ggcccaagta	aagcacagcg	cgggagccta	gagcacatga	agctgaccc	180
gcgtgataag	gagaaggagg	tggaaatgtca	gcaggagcat	atccatgaac	tccaggagct	240
caaagaccag	ctggagcagc	agctccaggg	cctgcacagg	aaggtaggtg	agaccagcct	300
cctcctgtcc	cagcgagagc	aggaaatagt	ggtcctgcag	cagcaactgc	aggaagccag	360
ggaacaagg	gagctgaagg	agcagtcact	tcagagtcaa	ctggatgagg	cccagagagc	420
cctagcccag	ag					432

<210> 162

<211> 433

<212> DNA

<213> homo sapien

<400> 162

gattcggcac	gagccggagc	tgggttgctc	ctgctcccgt	ctccaagtec	tggtaacctcc	60
ttcaagctgg	gagagggctc	tagtccctgg	ttctgaacac	tctgggggtc	tgggtgagc	120
gccgccatga	gcaaaccgaa	ggcgccgcag	gagactctca	acgggggaat	caccgacatg	180
ctcacagaac	tcgcaaactt	tgagaagaac	gtgagccaag	ctatccacaa	gtacaatgct	240
tacagaaaag	cagcatctgt	tatagcaaaa	taccacaca	aaataaagag	tggagctgaa	300
gctaagaaat	tgcctggagt	aggaacaaaa	attgctgaaa	agattgatga	gtttttagca	360
actggaaaat	tacgtaaact	ggaaaagatt	cggcaggatg	atacgagttc	atccatcaat	420
ttcctgactc	gag					433

<210> 163

<211> 432

<212> DNA

<213> homo sapien

<400> 163

gaattcggca	ccagatgagg	ccaacgaggt	gacggacagc	gcgtacatgg	gctccgagag	60
cacctacagt	gagtgtgaga	ccttcacgga	cgaggacacc	agcaccctgg	tgcaccctga	120
gctgcaacct	gaaggggacg	cagacagtgc	cggcggtctg	gccgtgccct	ctgagtgcc	180
ggacgccatg	gaggagcccg	accatggtgc	cctgctgctg	ctcccaggca	ggcctcacc	240
ccatggccag	tctgtcatca	cggtgatcgg	ggcgaggagg	cactttgagg	actacggtga	300
aggcagttag	gcggagctgt	ccccagagac	cctatgcaac	gggcagctgg	gctgcagtga	360
ccccgctttc	ctcacgcccc	gtccgacaaa	gcggctctcc	agcaagaagg	tggcaaggta	420
cctgcaccag	tc					432

<210> 164

<211> 395

<212> DNA

<213> homo sapien

<400> 164

gacacttgaa	tcattgggtga	cgttaaaaat	tttctgtatg	cctgggtgtg	caaaaggaag	60
atgaccccat	cctatgaaat	tagagcagt	gggaacaaaa	acaggcagaa	attcatgtgt	120
gaggttcagg	tggaaaggta	taattacact	ggcatgggaa	attccaccaa	taaaaaagat	180
gcacaaagca	atgctgccag	agactttgtt	aactatattg	ttcgaataaa	tgaataaag	240
agtgaagaag	ttccagcttt	tggggtagca	tctccgcccc	cacttactga	tactcctgac	300
actacagcaa	atgctgaagg	catcttgttg	acatcgaata	tgactttgat	aataaatacc	360
ggttcctgaa	aaaaaaaaaa	aaaaaaaaac	tcgag			395

<210> 165
 <211> 503
 <212> DNA
 <213> homo sapien

<400> 165

gaattcggca ccaggaacgc tcggtgagag gcggaggagc ggtaactacc ccggttgccg	60
acagctcggc gctccttccc gctccctcac acaccggcct cagcccgac cggcagtaga	120
agatgggtgaa agaaacaact tactacgatg ttttgggggt caaacccaat gctactcagg	180
aagaattgaa aaaggcttat aggaactgg ccttgaagta ccacccgat aagaacccaa	240
atgaaggaga gaagtttaaa cagatttctc aagcttacga agttctctct gatgcaaaga	300
aaaggggaatt atatgacaaa ggaggagaac aggcaattaa agagggtgga gcagggtggc	360
gttttggtc ccccatggac atctttgata tgttttttgg aggaggagga aggatgcaga	420
gagaaaggag aggtaaaaat gttgtacatc agctctcagt aaccctagaa gacttatata	480
atggtgcaac aagaaaactg gct	503

<210> 166
 <211> 893
 <212> DNA
 <213> homo sapien

<400> 166

gaattcggca cgagaggaac ttctcttgac gagaagagag accaaggagg ccaagcaggg	60
gctggggccag aggtgccaac atggggaaac tgaggctcgg ctcggaaggg tgagagtga	120
actacatctc aaaaaaaaaa aaaaaaaaaa aaaagaaaga aaagaaaaga aaaaagaaag	180
aacggaagta gttgtaggta gtggtatggt ggtatgagtc tgttttctgt tacttataac	240
aacaacaaca acaaaaaaac ctgaaactgg gtaatttara aagaaaagga aaaaaagcag	300
aaaaaatca ggaagaagag aaaggaaaag aagacaaata aatgaaattt atgtattaca	360
gttctgaagg ctgagacatc ccagggtcaag ggtccacact tggcgagggc tttcttgctg	420
gtggagactc tttgtggagt cctgggacag tgcagaagga tcacgcctcc ctaccgctcc	480
aagcccagcc ctacgccatg gcatgcccc tggatcaggc cattggcctc ctctgggcca	540
tcttccacaa gtactccggc agggagggtg acaagcacac cctgagcaag aaggagctga	600
aggagctgat ccagaaggag ctccaccattg gctcgaagct gcaggatgct gaaattgcaa	660
ggctgatgga agacttggac cggacaagg accaggaggt gaacttccag gaggatgca	720
ccttccctggg ggccttggct ttgatctaca atgaagccct caagggtgga aaataaatag	780
ggaagatgga gacaccctct gggggtcctc tctgagtcaa atccagtggg gggtaattgt	840
acaataaatt ttttttggtc aaatttaaaa aaaaaaaaaa aaaaaaactc gag	893

<210> 167
 <211> 549
 <212> DNA
 <213> homo sapien

<400> 167

gaattcggca cgagcccaga tcccagggtc cgacagcgcc cggcccagat cccacgcct	60
gccaggagca agccgagagc cagccggccg gcgcactccg actccgagca gtctctgtcc	120
ttcgacccga gccccgcgcc ctttccggga cccctgcccc gcgggcagcg ctgccaacct	180
gccggccatg gagaccccg cccagcggcg cgccaccgc agcggggcgc aggccagctc	240
cactccgctg tcgcccaccc gcatcacccg gctgcaggag aaggaggacc tgcaggagct	300
caatgatcgc ttggcggtct acatcgaccg tgtgcgctcg ctggaaaagg agaacgcagg	360
gctgcgcctt cgcacaccc agtctgaaga ggtggtcagc cgcgaggtgt ccggcatcaa	420
ggccgcctac gaggccgagc tcggggatgc ccgcaagacc cttgactcag tagccaagga	480
gcgcgcccgc ctgcagctgg agctgagcaa agtgcgtgaa gagtttaagg agctgaaagc	540
gcgcaatac	549

<210> 168
<211> 547
<212> DNA
<213> homo sapien

<400> 168
gaattcggca cgagatggcg gcaggggctcg aagcggcggc ggaggtggcg gcgacggaga 60
tcaaaatgga ggaagagagc ggcgcgcccc gcgtgccgag cggcaacggg gctccggggc 120
ctaaggggtga aggagaacga cctgctcaga atgagaagag gaaggagaaa aacataaaaa 180
gaggaggcaa tcgctttgag ccatatgcc aatcaactaa aagatacaga gccttcatta 240
caaacatacc ttttgatgtg aaatggcagt cacttaaaga cctgggttaa gaaaaagttg 300
gtgaggtaac atacgtggag ctcttaatgg acgctgaagg aaagtcaagg ggatgtgctg 360
ttgttgaatt caagatggaa gagagcatga aaaaagctgc ggaagtccta aacaagcata 420
gtctgagcgg aagaccactg aaagtcaaag aagatcctga tggatgaacat gccaggagag 480
caatgcaaaa ggctggaaga cttggaagca cagtatttct agcaaactct gattataaag 540
ttggctg 547

<210> 169
<211> 547
<212> DNA
<213> homo sapien

<400> 169
gaattcggca ccaggagtcc gactgtgctc gctgctcagc gccgcacccg gaagatgagg 60
ctcgccgtgg gagccctgct ggtctgcgcc gtcctggggc tgtgtctggc tgtccctgat 120
aaaactgtga gatggtgtgc agtgcctggag catgaggcca ctaagtcca gagtttccgc 180
gaccatatga aaagcgtcat tccatccgat ggtcccagtg ttgcttgtgt gaagaaagcc 240
tcctaccttg attgcatcag ggccattgag gcaaacgaag cggatgctgt gacactggat 300
gcaggtttgg tgtatgatgc ttacctggct cccaataacc tgaagcctgt ggtggcagag 360
ttctatgggt caaaagagga tccacagact ttctattatg ctgttgctgt ggtgaagaag 420
gatagtggct tccagatgaa ccagcttcga ggcaagaagt cctgccacac ggggtctaggc 480
aggctccgctg ggtggaacat ccccataggc ttactttact gtgacttacc tgagccacgt 540
aaacctc 547

<210> 170
<211> 838
<212> DNA
<213> homo sapien

<400> 170
gaattcggca ccagaggagc tcggcctgag ctgcgccacg atgtccgggg agtcagccag 60
gagcttgggg aaggggaagc cgccccggg gccggtcccg gagggtcga tccgcatcta 120
cagcatgagg ttctgcccgt ttgctgagag gacgcgtcta gtcctgaagg ccaagggaat 180
caggcatgaa gtcataata tcaacctgaa aaataagcct gagtgggttct ttaagaaaaa 240
tccttttggg ctggtgccag ttctggaaaa cagtcagggg cagctgatct acgagtctgc 300
catcacctgt gagtacctgg atgaagcata cccaggggaag aagctgttgc cggatgacc 360
ctatgagaaa gcttgccaga agatgatctt agagttgttt tctaagggtgc catccttggg 420
aggaagcttt attagaagcc aaaataaaga agactatgat ggcctaaaag aagaatttcg 480
taaagaattt accaagctag aggaggttct gactaataag aagacgacct tctttgggtg 540
caattctatc tctatgattg attacctcat ctggccctgg tttgaacggc tgggaagcaat 600
gaagttaaat gagtgtgtag accacactcc aaaactgaaa ctgtggatgg cagccatgaa 660
ggaagatccc acagtctcag ccctgcttac tagtgagaaa gactggcaag gtttcttaga 720
gctctactta cagaacagcc ctgaggcctg tgactatggg ctctgaaggg ggcaggagtc 780
agcaataaag ctatgtctga tattttccct cactaaaaaa aaaaaaaaaa aactcgag 838

<210> 171
 <211> 547
 <212> DNA
 <213> homo sapien

<400> 171

gaattcggca ccagcgggat ttgggtcgca gttcttgttt gtggattgct gtgacgtca	60
cttgacaatg cagatcttcg tgaagactct gactggtaag accatcacc ctagggtga	120
gccagtgac accatcgaga atgtcaaggc aaagatccaa gataaggaag gcatccctcc	180
tgaccagcag aggctgatct ttgctggaaa acagctggaa gatgggcgca ccctgtctga	240
ctacaacatc cagaaagagt ccaccctgca cctgggtgctc cgtctcagag gtgggatgca	300
aatcttcgtg aagacactca ctggcaagac catcaccctt gaggtcgagc ccagtgcac	360
catcgagaac gtcaaagcaa agatccagga caaggaaggc attcctcctg accagcagag	420
gttgatcttt gccggaaagc agctggaaga tgggcgcacc ctgtctgact acaacatcca	480
gaaagagtct accctgcacc tgggtgctccg tctcagaggc gggatgcaga tcttcgtgaa	540
gaccctg	547

<210> 172
 <211> 608
 <212> DNA
 <213> homo sapien

<400> 172

gaattcggca ccagagactt ctccctctga ggctcgca cccctcctca tcagcctgtc	60
caccctcatc tacaatggtg ccctgccatg tcagtgaac cctcaaggct cactgagttc	120
tgagtgaac cctcatggtg gtcagtgcct gtgcaagcct ggagtggctg ggcgcgctg	180
tgacctctgt gcccctggct actatggctt tggccccaca ggctgtcaag gcgcttgct	240
gggtgcccgt gatcacacag ggggtgagca ctgtgaaagg tgcattgctg gtttccacgg	300
ggacccacgg ctgccatag ggggccagt cggccctgt ccctgtcctg aaggccctgg	360
gagccaacgg cactttgcta cttcttgcca ccaggatgaa tattcccagc agattgtgtg	420
ccactgccgg gcaggctata cggggctgct atgtgaagct tgtgccccctg ggcactttgg	480
ggacccatca aggccagggt gccggtgcca actgtgtgag tgcagtggga acattgacct	540
aatggatcct gatgcctgtg acccccacac ggggcaatgc ctgcgctgtg tacaccacac	600
agagggtc	608

<210> 173
 <211> 543
 <212> DNA
 <213> homo sapien

<400> 173

gaattcggca ccagagatca tccgccagca gggctctggcc tctacgact acgtgcgccc	60
ccgcctcagc gctgaggacc tgttcgaggc tcggatcacc tctctcgaga cctacaacct	120
gctccgggag ggcaccagga gcctccgtga ggctctcgag gcggagtccg cctgggtgcta	180
cctctatggc acgggctccg tggctgggtg ctacctgccc ggttccaggc agacactgag	240
catctaccag gctctcaaga aagggtcgtc gagtgcgag gtggcccgcc tgcgtctgga	300
ggcacaggca gccacaggct tcctgctgga ccggtgaag ggggaacggc tgactgtgga	360
tgaagctgtg cggaagggcc tcgtggggcc cgaactgcac gaccgcctgc tctcggctga	420
gcgggcgggt accggtacc gtgaccccta caccgagcag accatctcgc tcttccaggc	480
catgaagaag gaactgatcc ctactgagga ggccctgcgg ctgtggatgc ccagctggcc	540
acc	543

<210> 174
 <211> 548
 <212> DNA

<213> homo sapien

<400> 174

gaattcggca	cgagaaatgg	cggcaggggt	cgaagcggcg	gcggaggtgg	cggcgacgga	60
gatcaaaatg	gaggaagaga	gcggcgcgcc	cggcgtgccc	agcggcaacg	gggctccggg	120
ccctaagggt	gaaggagaac	gacctgctca	gaatgagaag	aggaaggaga	aaaacataaa	180
aagaggaggc	aatcgctttg	agccatatgc	caatccaact	aaaagataca	gagccttcat	240
tacaaacata	ccttttgatg	tgaaatggca	gtcacttaaa	gacctgggta	aagaaaaagt	300
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tggttggtgaa	ttcaagatgg	aagagagcat	gaaaaaagct	gcggaagtcc	taaacaagca	420
tagtctgagc	ggaagaccac	tgaaagtcaa	agaagatcct	gatggtgaac	atgccaggag	480
agcaatgcaa	aaggtgatgg	ctacgactgg	tgggatgggt	atgggaccag	gtggcccagg	540
aatgatta						548

<210> 175

<211> 604

<212> DNA

<213> homo sapien

<400> 175

gaattcggca	ccagaggacc	tccaggacat	gttcacgtgc	cataccatcg	aggagattga	60
gggcctgatc	tcagcccattg	accagttcaa	gtccaccctg	cggacgccc	ataggagcgg	120
cgaggccatc	ctggccatcc	acaaggaggc	ccagaggatc	gctgagagca	accacatcaa	180
gctgtcgggc	agcaacccct	acaccaccgt	caccccgcaa	atcatcaact	ccaagtggga	240
gaaggtgcag	cagctgggtgc	caaaacggga	ccatgccctc	ctggagagc	agagcaagca	300
gcagtccaac	gagcacctgc	gccgccagtt	cgccagccag	gccaatctg	tggggccctg	360
gatccagacc	aagatggagg	agatcgggcg	catctccatt	gagatgaacg	ggaccctgga	420
ggaccagctg	agccacctga	agcagtatga	acgcagcacc	gtggactaca	agcccaacct	480
ggacctgctg	gagcagcagc	accagcttat	ccaggaggcc	ctcatcttcg	acaacaagca	540
caccaactat	accatggagc	acatccgcgt	gggctgggag	cagctgctca	ccaccattgc	600
ccgg						604

<210> 176

<211> 486

<212> DNA

<213> homo sapien

<400> 176

gaattcggca	ccagccaagc	tcactattga	atccacgccc	ttcaatgtcg	cagaggggaa	60
ggaggttctt	ctactcgccc	acaacctgcc	ccagaatcgt	attgggttaca	gctggtacaa	120
aggcgaaaga	gtggatggca	acagtctaatt	tgtaggatat	gtaataggaa	ctcaacaagc	180
tacccagggg	cccgcatata	gtggctcgaga	gacaatatac	cccaatgcat	ccctgctgat	240
ccagaacgtc	accagaatg	acacaggatt	ctataacctta	caagtcataa	agtcagatct	300
tgtgaatgaa	gaagcaaccg	gacagttcca	tgtatacccg	gagctgccc	agccctccat	360
ctccagcaac	aactccaacc	ccgtggagga	caaggatgct	gtggccttca	cctgtgaacc	420
tgaggttcag	aacacaacct	acctgtgggtg	ggtaaatggt	cagagcctcc	cggtcagtc	480
caaggc						486

<210> 177

<211> 387

<212> DNA

<213> homo sapien

<400> 177

gaattcggca	ccaggggacag	cagaccagac	agtcacagca	gccttgacaa	aacgttccctg	60
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gaactcaagc	tcttctccac	agaggaggac	agagcagaca	gcagagacca	tggagtctcc	120
ctcggccccc	ccccacagat	ggtgcatccc	ctggcagagg	ctcctgctca	cagcctcact	180
tctaaccctt	tggaacccgc	ccaccactgc	caagctcact	attgaatcca	cgccgttcaa	240
tgtcgcagag	gggaaggagg	tgcttctact	tgtccacaat	ctgccccagc	atcttttttg	300
ctacagctgg	tacaaaagg	aaagagtga	tggcaaccgt	caaattatag	gatatgtaat	360
aggaactcaa	caagctaccc	cagggcc				387

<210> 178

<211> 440

<212> DNA

<213> homo sapien

<400> 178

gaattcggca	cgaggagaag	cagaaaaaca	aggaatttag	ccagacttta	gaaaatgaga	60
aaaatacctt	actgagtcag	atatcaacaa	aggatggtga	actaaaaatg	cttcaggagg	120
aagtaaccaa	aatgaacctg	ttaaatacag	aaatccaaga	agaactctct	agagttacca	180
aactaaagga	gacagcagaa	gaagagaaag	atgattttga	agagaggctt	atgaatcaat	240
tagcagaact	taatggaagc	attgggaatt	actgtcagga	tgttacagat	gccccaaata	300
aaaatgagct	attggaatct	gaaatgaaga	accttaaaaa	gtgtgtgagt	gaattggaag	360
aagaaaagca	gcagtttagt	aaggaaaaaa	ctaagggtga	atcagaaata	cgaaaggaat	420
atttggaaga	aatacaaggt					440

<210> 179

<211> 443

<212> DNA

<213> homo sapien

<400> 179

gaattcggca	ccagcggggg	gctacggcgg	cggctacggc	ggcgtcctga	ccgcgtccga	60
cgggctgctg	gcgggcaacg	agaagctaac	catgcagaac	ctcaacgacc	gcctggcctc	120
ctacctggac	aagggtgcgcg	ccctggaggc	ggccaacggc	gagctagagg	tgaagatccg	180
cgactggtac	cagaagcagg	ggcctgggcc	ctccgcgac	tacagccact	actacacgac	240
catccaggac	ctgcgggaca	agattcttgg	tgccaccatt	gagaactcca	ggattgtcct	300
gcagatcgac	aacgcccgtc	tggctgcaga	tgacttccga	accaagtctg	agacggaaca	360
ggctctgctg	atgagcgtgg	aggccgacat	caacggcctg	cgcaggggtg	tggatgagct	420
gaccctggcc	aggaccgacc	tgg				443

<210> 180

<211> 403

<212> DNA

<213> homo sapien

<400> 180

gaattcggca	cgaggttatg	agagtcgact	tcaatgttcc	tatgaagaac	aaccagataa	60
caaacaacca	gaggattaag	gctgctgtcc	caagcatcaa	attctgcttg	gacaatggag	120
ccaagtccgt	agtccttatg	agccacctag	gccggcctga	tgggtgtgcc	atgcctgaca	180
agtactcctt	agagccagtt	gctgtagaac	tcagatctct	gctgggcaag	gatgttctgt	240
tcttgaagga	ctgtgtaggc	ccagaagtgg	agaaagcctg	tgccaaccca	gctgctgggt	300
ctgtcatcct	gctggagaac	ctccgcttcc	atgtggagga	agaaggggaag	ggaaaagatg	360
cttctgggaa	caaggttaaa	gccgagccag	ccaaaataga	agc		403

<210> 181

<211> 493

<212> DNA

<213> homo sapien

<400> 181

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gaattcggca ccagcagagg tctccagagc cttctctctc ctgtgcaaaa tggcaactct      60
taaggaaaaa ctcattgcac cagttgcgga agaagaggca acagttccaa acaataagat      120
cactgtagtg ggtgttggaac aagttggtat ggcgtgtgct atcagcattc tgggaaagtc      180
tctggctgat gaacttgctc ttgtggatgt tttggaagat aagcttaaag gagaaatgat      240
ggatctgcag catgggagct tatttcttca gacacctaaa attgtggcag ataaagatta      300
ttctgtgacc gccaatctca agattgtagt ggtaactgca ggagtcctgc agcaagaagg      360
ggagagtcgg ctcaatctgg tgcagagaaa tgtaaatgtc ttcaaattca ttattcctca      420
gatcgtcaag tacagtcctg attgcatcat aattgtggtt tccaaccagc tggacattct      480
tacgtatggt acc                                     493

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<210> 182

<211> 209

<212> PRT

<213> homo sapien

<400> 182

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Ala Phe Ser Ser Asn Pro Lys Val Gln Val Glu Ala Ile Glu Gly Gly
 1           5           10           15
Ala Leu Gln Lys Leu Leu Val Ile Leu Ala Thr Glu Gln Pro Leu Thr
 20           25           30
Ala Lys Lys Lys Val Leu Phe Ala Leu Cys Ser Leu Leu Arg His Phe
 35           40           45
Pro Tyr Ala Gln Arg Gln Phe Leu Lys Leu Gly Gly Leu Gln Val Leu
 50           55           60
Arg Thr Leu Val Gln Glu Lys Gly Thr Glu Val Leu Ala Val Arg Val
 65           70           75           80
Val Thr Leu Leu Tyr Asp Leu Val Thr Glu Lys Met Phe Ala Glu Glu
 85           90           95
Glu Ala Glu Leu Thr Gln Glu Met Ser Pro Glu Lys Leu Gln Gln Tyr
100           105           110
Arg Gln Val His Leu Leu Pro Gly Leu Trp Glu Gln Gly Trp Cys Glu
115           120           125
Ile Thr Ala His Leu Leu Ala Leu Pro Glu His Asp Ala Arg Glu Lys
130           135           140
Val Leu Gln Thr Leu Gly Val Leu Leu Thr Thr Cys Arg Asp Arg Tyr
145           150           155           160
Arg Gln Asp Pro Gln Leu Gly Arg Thr Leu Ala Ser Leu Gln Ala Glu
165           170           175
Tyr Gln Val Leu Ala Ser Leu Glu Leu Gln Asp Gly Glu Asp Glu Gly
180           185           190
Tyr Phe Gln Glu Leu Leu Gly Ser Val Asn Ser Leu Leu Lys Glu Leu
195           200           205
Arg

```

<210> 183

<211> 255

<212> PRT

<213> homo sapien

<400> 183

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Met Ala Ala Gly Val Glu Ala Ala Ala Glu Val Ala Ala Thr Glu Pro
 1           5           10           15

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Lys Met Glu Glu Glu Ser Gly Ala Pro Cys Val Pro Ser Gly Asn Gly
 20 25 30
 Ala Pro Gly Pro Lys Gly Glu Glu Arg Pro Thr Gln Asn Glu Lys Arg
 35 40 45
 Lys Glu Lys Asn Ile Lys Arg Gly Gly Asn Arg Phe Glu Pro Tyr Ser
 50 55 60
 Asn Pro Thr Lys Arg Tyr Arg Ala Phe Ile Thr Asn Ile Pro Phe Asp
 65 70 75 80
 Val Lys Trp Gln Ser Leu Lys Asp Leu Val Lys Glu Lys Val Gly Glu
 85 90 95
 Val Thr Tyr Val Glu Leu Leu Met Asp Ala Glu Gly Lys Ser Arg Gly
 100 105 110
 Cys Ala Val Val Glu Phe Lys Met Glu Glu Ser Met Lys Lys Ala Ala
 115 120 125
 Glu Val Leu Asn Lys His Ser Leu Ser Gly Arg Pro Leu Lys Val Lys
 130 135 140
 Glu Asp Pro Asp Gly Glu His Ala Arg Arg Ala Met Gln Lys Ala Gly
 145 150 155 160
 Arg Leu Gly Ser Thr Val Phe Val Ala Asn Leu Asp Tyr Lys Val Gly
 165 170 175
 Trp Lys Lys Leu Lys Glu Val Phe Ser Met Ala Gly Val Val Arg
 180 185 190
 Ala Asp Ile Leu Glu Asp Lys Asp Gly Lys Ser Arg Gly Ile Gly Ile
 195 200 205
 Val Thr Phe Glu Gln Ser Ile Glu Ala Val Gln Ala Ile Ser Met Phe
 210 215 220
 Asn Gly Gln Leu Leu Phe Asp Arg Pro Met His Val Lys Met Asp Glu
 225 230 235 240
 Arg Ala Leu Pro Lys Gly Asp Phe Phe Pro Pro Glu Arg His Ser
 245 250 255

<210> 184
 <211> 188
 <212> PRT
 <213> Homo sapien

<400> 184
 Leu Ser Gly Ser Cys Ile Arg Arg Glu Gln Thr Pro Glu Lys Glu Lys
 1 5 10 15
 Gln Val Val Leu Phe Glu Glu Ala Ser Trp Thr Cys Thr Pro Ala Cys
 20 25 30
 Gly Asp Glu Pro Arg Thr Val Ile Leu Leu Ser Ser Met Leu Ala Asp
 35 40 45
 His Arg Leu Lys Leu Glu Asp Tyr Lys Asp Arg Leu Lys Ser Gly Glu
 50 55 60
 His Leu Asn Pro Asp Gln Leu Glu Ala Val Glu Lys Tyr Glu Glu Val
 65 70 75 80
 Leu His Asn Leu Glu Phe Ala Lys Glu Leu Gln Lys Thr Phe Ser Gly
 85 90 95
 Leu Ser Leu Asp Leu Leu Lys Ala Gln Lys Lys Ala Gln Arg Arg Glu
 100 105 110
 His Met Leu Lys Leu Glu Ala Glu Lys Lys Lys Leu Arg Thr Ile Leu
 115 120 125
 Gln Val Gln Tyr Val Leu Gln Asn Leu Thr Gln Glu His Val Gln Lys
 130 135 140

Asp Phe Lys Gly Gly Leu Asn Gly Ala Val Tyr Leu Pro Ser Lys Glu
 145 150 155 160
 Leu Asp Tyr Leu Ile Lys Phe Ser Lys Leu Thr Cys Pro Glu Arg Asn
 165 170 175
 Glu Ser Leu Arg Gln Thr Leu Glu Gly Ser Thr Val
 180 185

<210> 185
 <211> 746
 <212> PRT
 <213> Homo sapien

<400> 185
 Asp Lys His Leu Lys Asp Leu Leu Ser Lys Leu Leu Asn Ser Gly Tyr
 1 5 10 15
 Phe Glu Ser Ile Pro Val Pro Lys Asn Ala Lys Glu Lys Glu Val Pro
 20 25 30
 Leu Glu Glu Glu Met Leu Ile Gln Ser Glu Lys Lys Thr Gln Leu Ser
 35 40 45
 Lys Thr Glu Ser Val Lys Glu Ser Glu Ser Leu Met Glu Phe Ala Gln
 50 55 60
 Pro Glu Ile Gln Pro Gln Glu Phe Leu Asn Arg Arg Tyr Met Thr Glu
 65 70 75 80
 Val Asp Tyr Ser Asn Lys Gln Gly Glu Glu Gln Pro Trp Glu Ala Asp
 85 90 95
 Tyr Ala Arg Lys Pro Asn Leu Pro Lys Arg Trp Asp Met Leu Thr Glu
 100 105 110
 Pro Asp Gly Gln Glu Lys Lys Gln Glu Ser Phe Lys Ser Trp Glu Ala
 115 120 125
 Ser Gly Lys His Gln Glu Val Ser Lys Pro Ala Val Ser Leu Glu Gln
 130 135 140
 Arg Lys Gln Asp Thr Ser Lys Leu Arg Ser Thr Leu Pro Glu Glu Gln
 145 150 155 160
 Lys Lys Gln Glu Ile Ser Lys Ser Lys Pro Ser Pro Ser Gln Trp Lys
 165 170 175
 Gln Asp Thr Pro Lys Ser Lys Ala Gly Tyr Val Gln Glu Glu Gln Lys
 180 185 190
 Lys Gln Glu Thr Pro Lys Leu Trp Pro Val Gln Leu Gln Lys Glu Gln
 195 200 205
 Asp Pro Lys Lys Gln Thr Pro Lys Ser Trp Thr Pro Ser Met Gln Ser
 210 215 220
 Glu Gln Asn Thr Thr Lys Ser Trp Thr Thr Pro Met Cys Glu Glu Gln
 225 230 235 240
 Asp Ser Lys Gln Pro Glu Thr Pro Lys Ser Trp Glu Asn Asn Val Glu
 245 250 255
 Ser Gln Lys His Ser Leu Thr Ser Gln Ser Gln Ile Ser Pro Lys Ser
 260 265 270
 Trp Gly Val Ala Thr Ala Ser Leu Ile Pro Asn Asp Gln Leu Leu Pro
 275 280 285
 Arg Lys Leu Asn Thr Glu Pro Lys Asp Val Pro Lys Pro Val His Gln
 290 295 300
 Pro Val Gly Ser Ser Ser Thr Leu Pro Lys Asp Pro Val Leu Arg Lys
 305 310 315 320
 Glu Lys Leu Gln Asp Leu Met Thr Gln Ile Gln Gly Thr Cys Asn Phe
 325 330 335

Met Gln Glu Ser Val Leu Asp Phe Asp Lys Pro Ser Ser Ala Ile Pro
 340 345 350
 Thr Ser Gln Pro Pro Ser Ala Thr Pro Gly Ser Pro Val Ala Ser Lys
 355 360 365
 Glu Gln Asn Leu Ser Ser Gln Ser Asp Phe Leu Gln Glu Pro Leu Gln
 370 375 380
 Val Phe Asn Val Asn Ala Pro Leu Pro Pro Arg Lys Glu Gln Glu Ile
 385 390 395 400
 Lys Glu Ser Pro Tyr Ser Pro Gly Tyr Asn Gln Ser Phe Thr Thr Ala
 405 410 415
 Ser Thr Gln Thr Pro Pro Gln Cys Gln Leu Pro Ser Ile His Val Glu
 420 425 430
 Gln Thr Val His Ser Gln Glu Thr Ala Ala Asn Tyr His Pro Asp Gly
 435 440 445
 Thr Ile Gln Val Ser Asn Gly Ser Leu Ala Phe Tyr Pro Ala Gln Thr
 450 455 460
 Asn Val Phe Pro Arg Pro Thr Gln Pro Phe Val Asn Ser Arg Gly Ser
 465 470 475 480
 Val Arg Gly Cys Thr Arg Gly Gly Arg Leu Ile Thr Asn Ser Tyr Arg
 485 490 495
 Ser Pro Gly Gly Tyr Lys Gly Phe Asp Thr Tyr Arg Gly Leu Pro Ser
 500 505 510
 Ile Ser Asn Gly Asn Tyr Ser Gln Leu Gln Phe Gln Ala Arg Glu Tyr
 515 520 525
 Ser Gly Ala Pro Tyr Ser Gln Arg Asp Asn Phe Gln Gln Cys Tyr Lys
 530 535 540
 Arg Gly Gly Thr Ser Gly Gly Pro Arg Ala Asn Ser Arg Ala Gly Trp
 545 550 555 560
 Ser Asp Ser Ser Gln Val Ser Ser Pro Glu Arg Asp Asn Glu Thr Phe
 565 570 575
 Asn Ser Gly Asp Ser Gly Gln Gly Asp Ser Arg Ser Met Thr Pro Val
 580 585 590
 Asp Val Pro Val Thr Asn Pro Ala Ala Thr Ile Leu Pro Val His Val
 595 600 605
 Tyr Pro Leu Pro Gln Gln Met Arg Val Ala Phe Ser Ala Ala Arg Thr
 610 615 620
 Ser Asn Leu Ala Pro Gly Thr Leu Asp Gln Pro Ile Val Phe Asp Leu
 625 630 635 640
 Leu Leu Asn Asn Leu Gly Glu Thr Phe Asp Leu Gln Leu Gly Arg Phe
 645 650 655
 Asn Cys Pro Val Asn Gly Thr Tyr Val Phe Ile Phe His Met Leu Lys
 660 665 670
 Leu Ala Val Asn Val Pro Leu Tyr Val Asn Leu Met Lys Asn Glu Glu
 675 680 685
 Val Leu Val Ser Ala Tyr Ala Asn Asp Gly Ala Pro Asp His Glu Thr
 690 695 700
 Ala Ser Asn His Ala Ile Leu Gln Leu Phe Gln Gly Asp Gln Ile Trp
 705 710 715 720
 Leu Arg Leu His Arg Gly Ala Ile Tyr Gly Ser Ser Trp Lys Tyr Ser
 725 730 735
 Thr Phe Ser Gly Tyr Leu Leu Tyr Gln Asp
 740 745

<210> 186

<211> 705

<212> PRT

<213> Homo sapien

<400> 186

Ala Leu Leu Asn Val Arg Gln Pro Pro Ser Thr Thr Thr Phe Val Leu
 1 5 10 15
 Asn Gln Ile Asn His Leu Pro Pro Leu Gly Ser Thr Ile Val Met Thr
 20 25 30
 Lys Thr Pro Pro Val Thr Thr Asn Arg Gln Thr Ile Thr Leu Thr Lys
 35 40 45
 Phe Ile Gln Thr Thr Ala Ser Thr Arg Pro Ser Val Ser Ala Pro Thr
 50 55 60
 Val Arg Asn Ala Met Thr Ser Ala Pro Ser Lys Asp Gln Val Gln Leu
 65 70 75 80
 Lys Asp Leu Leu Lys Asn Asn Ser Leu Asn Glu Leu Met Lys Leu Lys
 85 90 95
 Pro Pro Ala Asn Ile Ala Gln Pro Val Ala Thr Ala Ala Thr Asp Val
 100 105 110
 Ser Asn Gly Thr Val Lys Lys Glu Ser Ser Asn Lys Glu Gly Ala Arg
 115 120 125
 Met Trp Ile Asn Asp Met Lys Met Arg Ser Phe Ser Pro Thr Met Lys
 130 135 140
 Val Pro Val Val Lys Glu Asp Asp Glu Pro Glu Glu Glu Asp Glu Glu
 145 150 155 160
 Glu Met Gly His Ala Glu Thr Tyr Ala Glu Tyr Met Pro Ile Lys Leu
 165 170 175
 Lys Ile Gly Leu Arg His Pro Asp Ala Val Val Glu Thr Ser Ser Leu
 180 185 190
 Ser Ser Val Thr Pro Pro Asp Val Trp Tyr Lys Thr Ser Ile Ser Glu
 195 200 205
 Glu Thr Ile Asp Asn Gly Trp Leu Ser Ala Leu Gln Leu Glu Ala Ile
 210 215 220
 Thr Tyr Ala Ala Gln Gln His Glu Thr Phe Leu Pro Asn Gly Asp Arg
 225 230 235 240
 Ala Gly Phe Leu Ile Gly Asp Gly Ala Gly Val Gly Lys Gly Arg Thr
 245 250 255
 Ile Ala Gly Ile Ile Tyr Glu Asn Tyr Leu Leu Ser Arg Lys Arg Ala
 260 265 270
 Leu Trp Phe Ser Val Ser Asn Asp Leu Lys Tyr Asp Ala Glu Arg Asp
 275 280 285
 Leu Arg Asp Ile Gly Ala Lys Asn Ile Leu Val His Ser Leu Asn Lys
 290 295 300
 Phe Lys Tyr Gly Lys Ile Ser Ser Lys His Asn Gly Ser Val Lys Lys
 305 310 315 320
 Gly Val Ile Phe Ala Thr Tyr Ser Ser Leu Ile Gly Glu Ser Gln Ser
 325 330 335
 Gly Gly Lys Tyr Lys Thr Arg Leu Lys Gln Leu Leu His Trp Cys Gly
 340 345 350
 Asp Asp Phe Asp Gly Val Ile Val Phe Asp Glu Cys His Lys Ala Lys
 355 360 365
 Asn Leu Cys Pro Val Gly Ser Ser Lys Pro Thr Lys Thr Gly Leu Ala
 370 375 380
 Val Leu Glu Leu Gln Asn Lys Leu Pro Lys Ala Arg Val Val Tyr Ala
 385 390 395 400
 Ser Ala Thr Gly Ala Ser Glu Pro Arg Asn Met Ala Tyr Met Asn Arg

405 410 415
 Leu Gly Ile Trp Gly Glu Gly Thr Pro Phe Arg Glu Phe Ser Asp Phe
 420 425 430
 Ile Gln Ala Val Glu Arg Arg Gly Val Gly Ala Met Glu Ile Val Ala
 435 440 445
 Met Asp Met Lys Leu Arg Gly Met Tyr Ile Ala Arg Gln Leu Ser Phe
 450 455 460
 Thr Gly Val Thr Phe Lys Ile Glu Glu Val Leu Leu Ser Gln Ser Tyr
 465 470 475 480
 Val Lys Met Tyr Asn Lys Ala Val Lys Leu Trp Val Ile Ala Arg Glu
 485 490 495
 Arg Phe Gln Gln Ala Ala Asp Leu Ile Asp Ala Glu Gln Arg Met Lys
 500 505 510
 Lys Ser Met Trp Gly Gln Phe Trp Ser Ala His Gln Arg Phe Phe Lys
 515 520 525
 Tyr Leu Cys Ile Ala Ser Lys Val Lys Arg Val Val Gln Leu Ala Arg
 530 535 540
 Glu Glu Ile Lys Asn Gly Lys Cys Val Val Ile Gly Leu Gln Ser Thr
 545 550 555 560
 Gly Glu Ala Arg Thr Leu Glu Ala Leu Glu Glu Gly Gly Gly Glu Leu
 565 570 575
 Asn Asp Phe Val Ser Thr Ala Lys Gly Val Leu Gln Ser Leu Ile Glu
 580 585 590
 Lys His Phe Pro Ala Pro Asp Arg Lys Lys Leu Tyr Ser Leu Leu Gly
 595 600 605
 Ile Asp Leu Thr Ala Pro Ser Asn Asn Ser Ser Pro Arg Asp Ser Pro
 610 615 620
 Cys Lys Glu Asn Lys Ile Lys Lys Arg Lys Gly Glu Glu Ile Thr Arg
 625 630 635 640
 Glu Ala Lys Lys Ala Arg Lys Val Gly Gly Leu Thr Gly Ser Ser Ser
 645 650 655
 Asp Asp Ser Gly Ser Glu Ser Asp Ala Ser Asp Asn Glu Glu Ser Asp
 660 665 670
 Tyr Glu Ser Ser Lys Asn Met Ser Ser Gly Asp Asp Asp Phe Asn
 675 680 685
 Pro Phe Leu Asp Glu Ser Asn Glu Asp Asp Glu Asn Asp Pro Trp Leu
 690 695 700
 Ile
 705

<210> 187

<211> 595

<212> PRT

<213> Homo sapien

<400> 187

Glu Ser Pro Arg His Arg Gly Glu Gly Gly Glu Trp Gly Pro Gly
 1 5 10 15
 Val Pro Arg Glu Arg Arg Glu Ser Ala Gly Glu Trp Gly Ala Asp Thr
 20 25 30
 Pro Lys Glu Gly Gly Glu Ser Ala Gly Glu Trp Gly Ala Glu Val Pro
 35 40 45
 Arg Gly Arg Gly Glu Gly Ala Gly Glu Trp Gly Pro Asp Thr Pro Lys
 50 55 60
 Glu Arg Gly Gln Gly Val Arg Glu Trp Gly Pro Glu Ile Pro Gln Glu

65		70		75		80
His Gly Glu Ala Thr Arg Asp Trp Ala Leu Glu Ser Pro Arg Ala Leu						
	85			90		95
Gly Glu Asp Ala Arg Glu Leu Gly Ser Ser Pro His Asp Arg Gly Ala						
	100			105		110
Ser Pro Arg Asp Leu Ser Gly Glu Ser Pro Cys Thr Gln Arg Ser Gly						
	115			120		125
Leu Leu Pro Glu Arg Arg Gly Asp Ser Pro Trp Pro Pro Trp Pro Ser						
	130			135		140
Pro Gln Glu Arg Asp Ala Gly Thr Arg Asp Arg Glu Glu Ser Pro Arg						
145		150		155		160
Asp Trp Gly Gly Ala Glu Ser Pro Arg Gly Trp Glu Ala Gly Pro Arg						
	165			170		175
Glu Trp Gly Pro Ser Pro Ser Gly His Gly Asp Gly Pro Arg Arg Arg						
	180			185		190
Pro Arg Lys Arg Arg Gly Arg Lys Gly Arg Met Gly Arg Gln His Glu						
	195			200		205
Ala Ala Ala Thr Ala Ala Thr Ala Ala Thr Ala Thr Gly Gly Thr Ala						
	210			215		220
Glu Glu Ala Gly Ala Ser Ala Pro Glu Ser Gln Ala Gly Gly Gly Pro						
225		230		235		240
Arg Gly Arg Ala Arg Gly Pro Arg Gln Gln Gly Arg Arg Arg His Gly						
	245			250		255
Thr Gln Arg Arg Arg Gly Pro Pro Gln Ala Arg Glu Glu Gly Pro Arg						
	260			265		270
Asp Ala Thr Thr Ile Leu Gly Leu Gly Thr Pro Ser Gly Glu Gln Arg						
	275			280		285
Ala Asp Gln Ser Gln Ala Leu Pro Ala Leu Ala Gly Ala Ala Ala Ala						
	290			295		300
His Ala His Ala Ile Pro Gly Ala Gly Pro Ala Ala Ala Pro Val Gly						
305		310		315		320
Gly Arg Gly Arg Arg Gly Gly Trp Arg Gly Gly Arg Arg Gly Gly Ser						
	325			330		335
Ala Gly Ala Gly Gly Gly Gly Arg Gly Gly Arg Gly Arg Gly Arg Gly						
	340			345		350
Gly Gly Arg Gly Gly Gly Gly Ala Gly Arg Gly Gly Gly Ala Ala Gly						
	355			360		365
Pro Arg Glu Gly Ala Ser Ser Pro Gly Ala Arg Arg Gly Glu Gln Arg						
	370			375		380
Arg Arg Gly Arg Gly Pro Pro Ala Ala Gly Ala Ala Gln Val Ser Ala						
385		390		395		400
Arg Gly Arg Arg Ala Arg Gly Gln Arg Ala Gly Glu Glu Ala Gln Asp						
	405			410		415
Gly Leu Leu Pro Arg Gly Arg Asp Arg Leu Pro Leu Arg Pro Gly Asp						
	420			425		430
Ala Asn Gln Arg Ala Glu Arg Pro Gly Pro Pro Arg Gly Gly His Gly						
	435			440		445
Pro Val Asn Ala Ser Ser Ala Pro Asp Thr Ser Pro Pro Arg His Pro						
	450			455		460
Arg Arg Trp Val Ser Gln Gln Arg Gln Arg Leu Trp Arg Gln Phe Arg						
465		470		475		480
Val Gly Gly Gly Phe Pro Pro Pro Pro Ser Arg Pro Pro Ala Val						
	485			490		495
Leu Leu Pro Leu Arg Leu Ala Cys Ala Gly Asp Pro Gly Ala Thr						
	500			505		510

Arg Pro Gly Pro Arg Arg Pro Ala Arg Arg Pro Arg Gly Glu Leu Ile
 515 520 525
 Pro Arg Arg Pro Asp Pro Ala Ala Pro Ser Glu Glu Gly Leu Arg Met
 530 535 540
 Glu Ser Ser Val Asp Asp Gly Ala Thr Ala Thr Thr Ala Asp Ala Ala
 545 550 555 560
 Ser Gly Glu Ala Pro Glu Ala Gly Pro Ser Pro Ser His Ser Pro Thr
 565 570 575
 Met Cys Gln Thr Gly Gly Pro Gly Pro Pro Pro Pro Gln Pro Pro Arg
 580 585 590
 Trp Leu Pro
 595

<210> 188
 <211> 376
 <212> PRT
 <213> Homo sapien

<400> 188
 Glu Met Arg Lys Phe Asp Val Pro Ser Met Glu Ser Thr Leu Asn Gln
 1 5 10 15
 Pro Ala Met Leu Glu Thr Leu Tyr Ser Asp Pro His Tyr Arg Ala His
 20 25 30
 Phe Pro Asn Pro Arg Pro Asp Thr Asn Lys Asp Val Tyr Lys Val Leu
 35 40 45
 Pro Glu Ser Lys Lys Ala Pro Gly Ser Gly Ala Val Phe Glu Arg Asn
 50 55 60
 Gly Pro His Ala Ser Ser Ser Gly Val Leu Pro Leu Gly Leu Gln Pro
 65 70 75 80
 Ala Pro Gly Leu Ser Lys Ser Leu Ser Ser Gln Val Trp Gln Pro Ser
 85 90 95
 Pro Asp Pro Trp His Pro Gly Glu Gln Ser Cys Glu Leu Ser Thr Cys
 100 105 110
 Arg Gln Gln Leu Glu Leu Ile Arg Leu Gln Met Glu Gln Met Gln Leu
 115 120 125
 Gln Asn Gly Ala Met Cys His His Pro Ala Ala Phe Ala Pro Leu Leu
 130 135 140
 Pro Thr Leu Glu Pro Ala Gln Trp Leu Ser Ile Leu Asn Ser Asn Glu
 145 150 155 160
 His Leu Leu Lys Glu Lys Glu Leu Leu Ile Asp Lys Gln Arg Lys His
 165 170 175
 Ile Ser Gln Leu Glu Gln Lys Val Arg Glu Ser Glu Leu Gln Val His
 180 185 190
 Ser Ala Leu Leu Gly Arg Pro Ala Pro Phe Gly Asp Val Cys Leu Leu
 195 200 205
 Arg Leu Gln Glu Leu Gln Arg Glu Asn Thr Phe Leu Arg Ala Gln Phe
 210 215 220
 Ala Gln Lys Thr Glu Ala Leu Ser Lys Glu Lys Met Glu Leu Glu Lys
 225 230 235 240
 Lys Leu Ser Ala Ser Glu Val Glu Ile Gln Leu Ile Arg Glu Ser Leu
 245 250 255
 Lys Val Thr Leu Gln Lys His Ser Glu Glu Gly Lys Lys Gln Glu Glu
 260 265 270
 Arg Val Lys Gly Arg Asp Lys His Ile Asn Asn Leu Lys Lys Lys Cys
 275 280 285

Gln Lys Glu Ser Glu Gln Asn Arg Glu Lys Gln Gln Arg Ile Glu Thr
 290 295 300
 Leu Glu Arg Tyr Leu Ala Asp Leu Pro Thr Leu Glu Asp His Gln Lys
 305 310 315 320
 Gln Thr Glu Gln Leu Lys Asp Ala Glu Leu Lys Asn Thr Glu Leu Gln
 325 330 335
 Glu Arg Val Ala Glu Leu Glu Thr Leu Leu Glu Asp Thr Gln Ala Thr
 340 345 350
 Cys Arg Glu Lys Glu Val Gln Leu Glu Ser Leu Arg Gln Arg Glu Ala
 355 360 365
 Asp Leu Ser Ser Ala Arg His Arg
 370 375

<210> 189

<211> 160

<212> PRT

<213> Homo sapien

<400> 189

Met Leu Glu Ala His Arg Arg Gln Arg His Pro Phe Leu Leu Leu Gly
 1 5 10 15
 Thr Thr Ala Asn Arg Thr Gln Ser Leu Asn Tyr Gly Cys Ile Val Glu
 20 25 30
 Asn Pro Gln Thr His Glu Val Leu His Tyr Val Glu Lys Pro Ser Thr
 35 40 45
 Phe Ile Ser Asp Ile Ile Asn Cys Gly Ile Tyr Leu Phe Ser Pro Glu
 50 55 60
 Ala Leu Lys Pro Leu Arg Asp Val Phe Gln Arg Asn Gln Gln Asp Gly
 65 70 75 80
 Gln Leu Glu Asp Ser Pro Gly Leu Trp Pro Gly Ala Gly Thr Ile Arg
 85 90 95
 Leu Glu Gln Asp Val Phe Ser Ala Leu Ala Gly Gln Gly Gln Ile Tyr
 100 105 110
 Val His Leu Thr Asp Gly Ile Trp Ser Gln Ile Lys Ser Ala Gly Ser
 115 120 125
 Ala Leu Tyr Ala Ser Arg Leu Tyr Leu Ser Arg Tyr Gln Asp Thr His
 130 135 140
 Pro Glu Arg Leu Ala Lys His Thr Pro Gly Gly Pro Trp Ile Arg Gly
 145 150 155 160

<210> 190

<211> 146

<212> PRT

<213> Homo sapien

<400> 190

Met Asp Pro Arg Ala Ser Leu Leu Leu Leu Gly Asn Val Tyr Ile His
 1 5 10 15
 Pro Thr Ala Lys Val Ala Pro Ser Ala Val Leu Gly Pro Asn Val Ser
 20 25 30
 Ile Gly Lys Gly Val Thr Val Gly Glu Gly Val Arg Leu Arg Glu Ser
 35 40 45
 Ile Val Leu His Gly Ala Thr Leu Gln Glu His Thr Cys Val Leu His
 50 55 60
 Ser Ile Val Gly Trp Gly Ser Thr Val Gly Arg Trp Ala Arg Val Glu

[illegible]

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<210> 191
<211> 704
<212> PRT
<213> Homo sapien
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	<400>	191															
Glu	Gly	Gly	Cys	Ala	Ala	Gly	Arg	Gly	Arg	Glu	Leu	Glu	Pro	Glu	Leu		
1				5					10					15			
Glu	Pro	Gly	Pro	Gly	Pro	Gly	Ser	Ala	Leu	Glu	Pro	Gly	Glu	Glu	Phe		
			20					25					30				
Glu	Ile	Val	Asp	Arg	Ser	Gln	Leu	Pro	Gly	Pro	Gly	Asp	Leu	Arg	Ser		
		35				40						45					
Ala	Thr	Arg	Pro	Arg	Ala	Ala	Glu	Gly	Trp	Ser	Ala	Pro	Ile	Leu	Thr		
	50					55					60						
Leu	Ala	Arg	Arg	Ala	Thr	Gly	Asn	Leu	Ser	Ala	Ser	Cys	Gly	Ser	Ala		
65					70					75					80		
Leu	Arg	Ala	Ala	Ala	Gly	Leu	Gly	Gly	Gly	Asp	Ser	Gly	Asp	Gly	Thr		
				85				90						95			
Ala	Arg	Ala	Ala	Ser	Lys	Cys	Gln	Met	Met	Glu	Glu	Arg	Ala	Asn	Leu		
			100					105					110				
Met	His	Met	Met	Lys	Leu	Ser	Ile	Lys	Val	Leu	Leu	Gln	Ser	Ala	Leu		
	115						120					125					
Ser	Leu	Gly	Arg	Ser	Leu	Asp	Ala	Asp	His	Ala	Pro	Leu	Gln	Gln	Phe		
	130				135					140							
Phe	Val	Val	Met	Glu	His	Cys	Leu	Lys	His	Gly	Leu	Lys	Val	Lys	Lys		
145					150					155					160		
Ser	Phe	Ile	Gly	Gln	Asn	Lys	Ser	Phe	Phe	Gly	Pro	Leu	Glu	Leu	Val		
				165					170					175			
Glu	Lys	Leu	Cys	Pro	Glu	Ala	Ser	Asp	Ile	Ala	Thr	Ser	Val	Arg	Asn		
			180					185					190				
Leu	Pro	Glu	Leu	Lys	Thr	Ala	Val	Gly	Arg	Gly	Arg	Ala	Trp	Leu	Tyr		
		195				200						205					
Leu	Ala	Leu	Met	Gln	Lys	Lys	Leu	Ala	Asp	Tyr	Leu	Lys	Val	Leu	Ile		
	210					215					220						
Asp	Asn	Lys	His	Leu	Leu	Ser	Glu	Phe	Tyr	Glu	Pro	Glu	Ala	Leu	Met		
225					230					235					240		
Met	Glu	Glu	Glu	Gly	Met	Val	Ile	Val	Gly	Leu	Leu	Val	Gly	Leu	Asn		
				245					250					255			
Val	Leu	Asp	Ala	Asn	Leu	Cys	Leu	Lys	Gly	Glu	Asp	Leu	Asp	Ser	Gln		
			260					265					270				
Val	Gly	Val	Ile	Asp	Phe	Ser	Leu	Tyr	Leu	Lys	Asp	Val	Gln	Asp	Leu		
		275					280					285					
Asp	Gly	Gly	Lys	Glu	His	Glu	Arg	Ile	Thr	Asp	Val	Leu	Asp	Gln	Lys		

290 295 300
 Asn Tyr Val Glu Glu Leu Asn Arg His Leu Ser Cys Thr Val Gly Asp
 305 310 315 320
 Leu Gln Thr Lys Ile Asp Gly Leu Glu Lys Thr Asn Ser Lys Leu Gln
 325 330 335
 Glu Glu Leu Ser Ala Ala Thr Asp Arg Ile Cys Ser Leu Gln Glu Glu
 340 345 350
 Gln Gln Gln Leu Arg Glu Gln Asn Glu Leu Ile Arg Glu Arg Ser Glu
 355 360 365
 Lys Ser Val Glu Ile Thr Lys Gln Asp Thr Lys Val Glu Leu Glu Thr
 370 375 380
 Tyr Lys Gln Thr Arg Gln Gly Leu Asp Glu Met Tyr Ser Asp Val Trp
 385 390 395 400
 Lys Gln Leu Lys Glu Lys Lys Val Arg Leu Glu Leu Glu Lys Glu
 405 410 415
 Leu Glu Leu Gln Ile Gly Met Lys Thr Glu Met Glu Ile Ala Met Lys
 420 425 430
 Leu Leu Glu Lys Asp Thr His Glu Lys Gln Asp Thr Leu Val Ala Leu
 435 440 445
 Arg Gln Gln Leu Glu Glu Val Lys Ala Ile Asn Leu Gln Met Phe His
 450 455 460
 Lys Ala Gln Asn Ala Glu Ser Ser Leu Gln Gln Lys Asn Glu Ala Ile
 465 470 475 480
 Thr Ser Phe Glu Gly Lys Thr Asn Gln Val Met Ser Ser Met Lys Gln
 485 490 495
 Met Glu Glu Arg Leu Gln His Ser Glu Arg Ala Arg Gln Gly Ala Glu
 500 505 510
 Glu Arg Ser His Lys Leu Gln Gln Glu Leu Gly Gly Arg Ile Gly Ala
 515 520 525
 Leu Gln Leu Gln Leu Ser Gln Leu His Glu Gln Cys Ser Ser Leu Glu
 530 535 540
 Lys Glu Leu Lys Ser Glu Lys Glu Gln Arg Gln Ala Leu Gln Arg Glu
 545 550 555 560
 Leu Gln His Glu Lys Asp Thr Ser Ser Leu Leu Arg Met Glu Leu Gln
 565 570 575
 Gln Val Glu Gly Leu Lys Lys Glu Leu Arg Glu Leu Gln Asp Glu Lys
 580 585 590
 Ala Glu Leu Gln Lys Ile Cys Glu Glu Gln Glu Gln Ala Leu Gln Glu
 595 600 605
 Met Gly Leu His Leu Ser Gln Ser Lys Leu Lys Met Glu Asp Ile Lys
 610 615 620
 Glu Val Asn Gln Ala Leu Lys Gly His Ala Trp Leu Lys Asp Asp Glu
 625 630 635 640
 Ala Thr His Cys Arg Gln Cys Glu Lys Glu Phe Ser Ile Ser Arg Arg
 645 650 655
 Lys His His Cys Arg Asn Cys Gly His Ile Phe Cys Asn Thr Cys Ser
 660 665 670
 Ser Asn Glu Leu Ala Leu Pro Ser Tyr Pro Lys Pro Val Arg Val Cys
 675 680 685
 Asp Ser Cys His Thr Leu Leu Leu Gln Arg Cys Ser Ser Thr Ala Ser
 690 695 700

<210> 192

<211> 331

<212> PRT

<213> Homo sapien

<400> 192

Arg Ala Gly Ala Ser Ala Met Ala Leu Arg Lys Glu Leu Leu Lys Ser
 1 5 10 15
 Ile Trp Tyr Ala Phe Thr Ala Leu Asp Val Glu Lys Ser Gly Lys Val
 20 25 30
 Ser Lys Ser Gln Leu Lys Val Leu Ser His Asn Leu Tyr Thr Val Leu
 35 40 45
 His Ile Pro His Asp Pro Val Ala Leu Glu Glu His Phe Arg Asp Asp
 50 55 60
 Asp Asp Gly Pro Val Ser Ser Gln Gly Tyr Met Pro Tyr Leu Asn Lys
 65 70 75 80
 Tyr Ile Leu Asp Lys Val Glu Glu Gly Ala Phe Val Lys Glu His Phe
 85 90 95
 Asp Glu Leu Cys Trp Thr Leu Thr Ala Lys Lys Asn Tyr Arg Ala Asp
 100 105 110
 Ser Asn Gly Asn Ser Met Leu Ser Asn Gln Asp Ala Phe Arg Leu Trp
 115 120 125
 Cys Leu Phe Asn Phe Leu Ser Glu Asp Lys Tyr Pro Leu Ile Met Val
 130 135 140
 Pro Asp Glu Val Glu Tyr Leu Leu Lys Lys Val Leu Ser Ser Met Ser
 145 150 155 160
 Leu Glu Val Ser Leu Gly Glu Leu Glu Glu Leu Ala Gln Glu Ala
 165 170 175
 Gln Val Ala Gln Thr Thr Gly Gly Leu Ser Val Trp Gln Phe Leu Glu
 180 185 190
 Leu Phe Asn Ser Gly Arg Cys Leu Arg Gly Val Gly Arg Asp Thr Leu
 195 200 205
 Ser Met Ala Ile His Glu Val Tyr Gln Glu Leu Ile Gln Asp Val Leu
 210 215 220
 Lys Gln Gly Tyr Leu Trp Lys Arg Gly His Leu Arg Arg Asn Trp Ala
 225 230 235 240
 Glu Arg Trp Phe Gln Leu Gln Pro Ser Cys Leu Cys Tyr Phe Gly Ser
 245 250 255
 Glu Glu Cys Lys Glu Lys Arg Gly Ile Ile Pro Leu Asp Ala His Cys
 260 265 270
 Cys Val Glu Val Leu Pro Asp Arg Asp Gly Lys Arg Cys Met Phe Cys
 275 280 285
 Val Lys Thr Ala Thr Arg Thr Tyr Glu Met Ser Ala Ser Asp Thr Arg
 290 295 300
 Gln Arg Gln Glu Trp Thr Ala Ala Ile Gln Met Ala Ile Arg Leu Gln
 305 310 315 320
 Ala Glu Gly Lys Thr Ser Leu His Lys Asp Leu
 325 330

<210> 193

<211> 475

<212> PRT

<213> Homo sapien

<400> 193

Lys Asn Ser Pro Leu Leu Ser Val Ser Ser Gln Thr Ile Thr Lys Glu
 1 5 10 15
 Asn Asn Arg Asn Val His Leu Glu His Ser Glu Gln Asn Pro Gly Ser

20 25 30
 Ser Ala Gly Asp Thr Ser Ala Ala His Gln Val Val Leu Gly Glu Asn
 35 40 45
 Leu Ile Ala Thr Ala Leu Cys Leu Ser Gly Ser Gly Ser Gln Ser Asp
 50 55 60
 Leu Lys Asp Val Ala Ser Thr Ala Gly Glu Glu Gly Asp Thr Ser Leu
 65 70 75 80
 Arg Glu Ser Leu His Pro Val Thr Arg Ser Leu Lys Ala Gly Cys His
 85 90 95
 Thr Lys Gln Leu Ala Ser Arg Asn Cys Ser Glu Glu Lys Ser Pro Gln
 100 105 110
 Thr Ser Ile Leu Lys Glu Gly Asn Arg Asp Thr Ser Leu Asp Phe Arg
 115 120 125
 Pro Val Val Ser Pro Ala Asn Gly Val Glu Gly Val Arg Val Asp Gln
 130 135 140
 Asp Asp Asp Gln Asp Ser Ser Ser Leu Lys Leu Ser Gln Asn Ile Ala
 145 150 155 160
 Val Gln Thr Asp Phe Lys Thr Ala Asp Ser Glu Val Asn Thr Asp Gln
 165 170 175
 Asp Ile Glu Lys Asn Leu Asp Lys Met Met Thr Glu Arg Thr Leu Leu
 180 185 190
 Lys Glu Arg Tyr Gln Glu Val Leu Asp Lys Gln Arg Gln Val Glu Asn
 195 200 205
 Gln Leu Gln Val Gln Leu Lys Gln Leu Gln Gln Arg Arg Glu Glu Glu
 210 215 220
 Met Lys Asn His Gln Glu Ile Leu Lys Ala Ile Gln Asp Val Thr Ile
 225 230 235 240
 Lys Arg Glu Glu Thr Lys Lys Lys Ile Glu Lys Glu Lys Lys Glu Phe
 245 250 255
 Leu Gln Lys Glu Gln Asp Leu Lys Ala Glu Ile Glu Lys Leu Cys Glu
 260 265 270
 Lys Gly Arg Arg Glu Val Trp Glu Met Glu Leu Asp Arg Leu Lys Asn
 275 280 285
 Gln Asp Gly Glu Ile Asn Arg Asn Ile Met Glu Glu Thr Glu Arg Ala
 290 295 300
 Trp Lys Ala Glu Ile Leu Ser Leu Glu Ser Arg Lys Glu Leu Leu Val
 305 310 315 320
 Leu Lys Leu Glu Glu Ala Glu Lys Glu Ala Glu Leu His Leu Thr Tyr
 325 330 335
 Leu Lys Ser Thr Pro Pro Thr Leu Glu Thr Val Arg Ser Lys Gln Glu
 340 345 350
 Trp Glu Thr Arg Leu Asn Gly Val Arg Ile Met Lys Lys Asn Val Arg
 355 360 365
 Asp Gln Phe Asn Ser His Ile Gln Leu Val Arg Asn Gly Ala Lys Leu
 370 375 380
 Ser Ser Leu Pro Gln Ile Pro Thr Pro Thr Leu Pro Pro Pro Ser
 385 390 395 400
 Glu Thr Asp Phe Met Leu Gln Val Phe Gln Pro Ser Pro Ser Leu Ala
 405 410 415
 Pro Arg Met Pro Phe Ser Ile Gly Gln Val Thr Met Pro Met Val Met
 420 425 430
 Pro Ser Ala Asp Pro Arg Ser Leu Ser Phe Pro Ile Leu Asn Pro Ala
 435 440 445
 Leu Ser Gln Pro Ser Gln Pro Ser Ser Pro Leu Pro Gly Ser His Gly
 450 455 460

Arg Asn Ser Pro Gly Leu Gly Ser Leu Val Ser
 465 470 475

<210> 194
 <211> 241
 <212> PRT
 <213> Homo sapien

<400> 194
 Met Ser Gly Glu Ser Ala Arg Ser Leu Gly Lys Gly Ser Ala Pro Pro
 1 5 10 15
 Gly Pro Val Pro Glu Gly Ser Ile Arg Ile Tyr Ser Met Arg Phe Cys
 20 25 30
 Pro Phe Ala Glu Arg Thr Arg Leu Val Leu Lys Ala Lys Gly Ile Arg
 35 40 45
 His Glu Val Ile Asn Ile Asn Leu Lys Asn Lys Pro Glu Trp Phe Phe
 50 55 60
 Lys Lys Asn Pro Phe Gly Leu Val Pro Val Leu Glu Asn Ser Gln Gly
 65 70 75 80
 Gln Leu Ile Tyr Glu Ser Ala Ile Thr Cys Glu Tyr Leu Asp Glu Ala
 85 90 95
 Tyr Pro Gly Lys Lys Leu Leu Pro Asp Asp Pro Tyr Glu Lys Ala Cys
 100 105 110
 Gln Lys Met Ile Leu Glu Leu Phe Ser Lys Val Pro Ser Leu Val Gly
 115 120 125
 Ser Phe Ile Arg Ser Gln Asn Lys Glu Asp Tyr Ala Gly Leu Lys Glu
 130 135 140
 Glu Phe Arg Lys Glu Phe Thr Lys Leu Glu Glu Val Leu Thr Asn Lys
 145 150 155 160
 Lys Thr Thr Phe Phe Gly Gly Asn Ser Ile Ser Met Ile Asp Tyr Leu
 165 170 175
 Ile Trp Pro Trp Phe Glu Arg Leu Glu Ala Met Lys Leu Asn Glu Cys
 180 185 190
 Val Asp His Thr Pro Lys Leu Lys Leu Trp Met Ala Ala Met Lys Glu
 195 200 205
 Asp Pro Thr Val Ser Ala Leu Leu Thr Ser Glu Lys Asp Trp Gln Gly
 210 215 220
 Phe Leu Glu Leu Tyr Leu Gln Asn Ser Pro Glu Ala Cys Asp Tyr Gly
 225 230 235 240
 Leu

<210> 195
 <211> 138
 <212> PRT
 <213> Homo sapien

<400> 195
 Gln Thr Lys Ile Leu Glu Glu Asp Leu Glu Gln Ile Lys Leu Ser Leu
 1 5 10 15
 Arg Glu Arg Gly Arg Glu Leu Thr Thr Gln Arg Gln Leu Met Gln Glu
 20 25 30
 Arg Ala Glu Glu Gly Lys Gly Pro Ser Lys Ala Gln Arg Gly Ser Leu
 35 40 45
 Glu His Met Lys Leu Ile Leu Arg Asp Lys Glu Lys Glu Val Glu Cys

50 55 60
 Gln Gln Glu His Ile His Glu Leu Gln Glu Leu Lys Asp Gln Leu Glu
 65 70 75 80
 Gln Gln Leu Gln Gly Leu His Arg Lys Val Gly Glu Thr Ser Leu Leu
 85 90 95
 Leu Ser Gln Arg Glu Gln Glu Ile Val Val Leu Gln Gln Gln Leu Gln
 100 105 110
 Glu Ala Arg Glu Gln Gly Glu Leu Lys Glu Gln Ser Leu Gln Ser Gln
 115 120 125
 Leu Asp Glu Ala Gln Arg Ala Leu Ala Gln
 130 135

<210> 196
 <211> 102
 <212> PRT
 <213> Homo sapien

<400> 196
 Met Ser Lys Arg Lys Ala Pro Gln Glu Thr Leu Asn Gly-Gly Ile Thr
 1 5 10 15
 Asp Met Leu Thr Glu Leu Ala Asn Phe Glu Lys Asn Val Ser Gln Ala
 20 25 30
 Ile His Lys Tyr Asn Ala Tyr Arg Lys Ala Ala Ser Val Ile Ala Lys
 35 40 45
 Tyr Pro His Lys Ile Lys Ser Gly Ala Glu Ala Lys Lys Leu Pro Gly
 50 55 60
 Val Gly Thr Lys Ile Ala Glu Lys Ile Asp Glu Phe Leu Ala Thr Gly
 65 70 75 80
 Lys Leu Arg Lys Leu Glu Lys Ile Arg Gln Asp Asp Thr Ser Ser Ser
 85 90 95
 Ile Asn Phe Leu Thr Arg
 100

<210> 197
 <211> 138
 <212> PRT
 <213> Homo sapien

<400> 197
 Glu Ala Asn Glu Val Thr Asp Ser Ala Tyr Met Gly Ser Glu Ser Thr
 1 5 10 15
 Tyr Ser Glu Cys Glu Thr Phe Thr Asp Glu Asp Thr Ser Thr Leu Val
 20 25 30
 His Pro Glu Leu Gln Pro Glu Gly Asp Ala Asp Ser Ala Gly Gly Ser
 35 40 45
 Ala Val Pro Ser Glu Cys Leu Asp Ala Met Glu Glu Pro Asp His Gly
 50 55 60
 Ala Leu Leu Leu Leu Pro Gly Arg Pro His Pro His Gly Gln Ser Val
 65 70 75 80
 Ile Thr Val Ile Gly Gly Glu Glu His Phe Glu Asp Tyr Gly Glu Gly
 85 90 95
 Ser Glu Ala Glu Leu Ser Pro Glu Thr Leu Cys Asn Gly Gln Leu Gly
 100 105 110
 Cys Ser Asp Pro Ala Phe Leu Thr Pro Ser Pro Thr Lys Arg Leu Ser
 115 120 125

Ser Lys Lys Val Ala Arg Tyr Leu His Gln
130 135

<210> 198
<211> 100
<212> PRT
<213> Homo sapien

<400> 198
Met Gly Asp Val Lys Asn Phe Leu Tyr Ala Trp Cys Gly Lys Arg Lys
1 5 10 15
Met Thr Pro Ser Tyr Glu Ile Arg Ala Val Gly Asn Lys Asn Arg Gln
20 25 30
Lys Phe Met Cys Glu Val Gln Val Glu Gly Tyr Asn Tyr Thr Gly Met
35 40 45
Gly Asn Ser Thr Asn Lys Lys Asp Ala Gln Ser Asn Ala Ala Arg Asp
50 55 60
Phe Val Asn Tyr Leu Val Arg Ile Asn Glu Ile Lys Ser Glu Glu Val
65 70 75 80
Pro Ala Phe Gly Val Ala Ser Pro Pro Pro Leu Thr Asp Thr Pro Asp
85 90 95
Thr Thr Ala Asn
100

<210> 199
<211> 127
<212> PRT
<213> Homo sapien

<400> 199
Met Val Lys Glu Thr Thr Tyr Tyr Asp Val Leu Gly Val Lys Pro Asn
1 5 10 15
Ala Thr Gln Glu Glu Leu Lys Lys Ala Tyr Arg Lys Leu Ala Leu Lys
20 25 30
Tyr His Pro Asp Lys Asn Pro Asn Glu Gly Glu Lys Phe Lys Gln Ile
35 40 45
Ser Gln Ala Tyr Glu Val Leu Ser Asp Ala Lys Lys Arg Glu Leu Tyr
50 55 60
Asp Lys Gly Gly Glu Gln Ala Ile Lys Glu Gly Gly Ala Gly Gly Gly
65 70 75 80
Phe Gly Ser Pro Met Asp Ile Phe Asp Met Phe Phe Gly Gly Gly Gly
85 90 95
Arg Met Gln Arg Glu Arg Arg Gly Lys Asn Val Val His Gln Leu Ser
100 105 110
Val Thr Leu Glu Asp Leu Tyr Asn Gly Ala Thr Arg Lys Leu Ala
115 120 125

<210> 200
<211> 90
<212> PRT
<213> Homo sapien

<400> 200
Met Ala Cys Pro Leu Asp Gln Ala Ile Gly Leu Leu Val Ala Ile Phe
1 5 10 15

His Lys Tyr Ser Gly Arg Glu Gly Asp Lys His Thr Leu Ser Lys Lys
 20 25 30
 Glu Leu Lys Glu Leu Ile Gln Lys Glu Leu Thr Ile Gly Ser Lys Leu
 35 40 45
 Gln Asp Ala Glu Ile Ala Arg Leu Met Glu Asp Leu Asp Arg Asn Lys
 50 55 60
 Asp Gln Glu Val Asn Phe Gln Glu Tyr Val Thr Phe Leu Gly Ala Leu
 65 70 75 80
 Ala Leu Ile Tyr Asn Glu Ala Leu Lys Gly
 85 90

<210> 201
 <211> 120
 <212> PRT
 <213> Homo sapien

<400> 201
 Met Glu Thr Pro Ser Gln Arg Arg Ala Thr Arg Ser Gly Ala Gln Ala
 1 5 10 15
 Ser Ser Thr Pro Leu Ser Pro Thr Arg Ile Thr Arg Leu Gln Glu Lys
 20 25 30
 Glu Asp Leu Gln Glu Leu Asn Asp Arg Leu Ala Val Tyr Ile Asp Arg
 35 40 45
 Val Arg Ser Leu Glu Thr Glu Asn Ala Gly Leu Arg Leu Arg Ile Thr
 50 55 60
 Glu Ser Glu Glu Val Val Ser Arg Glu Val Ser Gly Ile Lys Ala Ala
 65 70 75 80
 Tyr Glu Ala Glu Leu Gly Asp Ala Arg Lys Thr Leu Asp Ser Val Ala
 85 90 95
 Lys Glu Arg Ala Arg Leu Gln Leu Glu Leu Ser Lys Val Arg Glu Glu
 100 105 110
 Phe Lys Glu Leu Lys Ala Arg Asn
 115 120

<210> 202
 <211> 177
 <212> PRT
 <213> Homo sapien

<400> 202
 Met Ala Ala Gly Val Glu Ala Ala Ala Glu Val Ala Ala Thr Glu Ile
 1 5 10 15
 Lys Met Glu Glu Ser Gly Ala Pro Gly Val Pro Ser Gly Asn Gly
 20 25 30
 Ala Pro Gly Pro Lys Gly Glu Gly Arg Pro Ala Gln Asn Glu Lys
 35 40 45
 Arg Lys Glu Lys Asn Ile Lys Arg Gly Gly Asn Arg Phe Glu Pro Tyr
 50 55 60
 Ala Asn Pro Thr Lys Arg Tyr Arg Ala Phe Ile Thr Asn Ile Pro Phe
 65 70 75 80
 Asp Val Lys Trp Gln Ser Leu Lys Asp Leu Val Lys Glu Lys Val Gly
 85 90 95
 Glu Val Thr Tyr Val Glu Leu Leu Met Asp Ala Glu Gly Lys Ser Arg
 100 105 110
 Gly Cys Ala Val Val Glu Phe Lys Met Glu Glu Ser Met Lys Lys Ala

115 120 125
 Ala Glu Val Leu Asn Lys His Ser Leu Ser Gly Arg Pro Leu Lys Val
 130 135 140
 Lys Glu Asp Pro Asp Gly Glu His Ala Arg Arg Ala Met Gln Lys Ala
 145 150 155 160
 Gly Arg Leu Gly Ser Thr Val Phe Val Ala Asn Leu Asp Tyr Lys Val
 165 170 175
 Gly

<210> 203
 <211> 164
 <212> PRT
 <213> Homo sapien

<400> 203
 Met Arg Leu Ala Val Gly Ala Leu Leu Val Cys Ala Val Leu Gly Leu
 1 5 10 15
 Cys Leu Ala Val Pro Asp Lys Thr Val Arg Trp Cys Ala Val Ser Glu
 20 25 30
 His Glu Ala Thr Lys Cys Gln Ser Phe Arg Asp His Met Lys Ser Val
 35 40 45
 Ile Pro Ser Asp Gly Pro Ser Val Ala Cys Val Lys Lys Ala Ser Tyr
 50 55 60
 Leu Asp Cys Ile Arg Ala Ile Ala Ala Asn Glu Ala Asp Ala Val Thr
 65 70 75 80
 Leu Asp Ala Gly Leu Val Tyr Asp Ala Tyr Leu Ala Pro Asn Asn Leu
 85 90 95
 Lys Pro Val Val Ala Glu Phe Tyr Gly Ser Lys Glu Asp Pro Gln Thr
 100 105 110
 Phe Tyr Tyr Ala Val Ala Val Val Lys Lys Asp Ser Gly Phe Gln Met
 115 120 125
 Asn Gln Leu Arg Gly Lys Lys Ser Cys His Thr Gly Leu Gly Arg Ser
 130 135 140
 Ala Gly Trp Asn Ile Pro Ile Gly Leu Leu Tyr Cys Asp Leu Pro Glu
 145 150 155 160
 Pro Arg Lys Pro

<210> 204
 <211> 241
 <212> PRT
 <213> Homo sapien

<400> 204
 Met Ser Gly Glu Ser Ala Arg Ser Leu Gly Lys Gly Ser Ala Pro Pro
 1 5 10 15
 Gly Pro Val Pro Glu Gly Ser Ile Arg Ile Tyr Ser Met Arg Phe Cys
 20 25 30
 Pro Phe Ala Glu Arg Thr Arg Leu Val Leu Lys Ala Lys Gly Ile Arg
 35 40 45
 His Glu Val Ile Asn Ile Asn Leu Lys Asn Lys Pro Glu Trp Phe Phe
 50 55 60
 Lys Lys Asn Pro Phe Gly Leu Val Pro Val Leu Glu Asn Ser Gln Gly
 65 70 75 80

Gln Leu Ile Tyr Glu Ser Ala Ile Thr Cys Glu Tyr Leu Asp Glu Ala
 85 90 95
 Tyr Pro Gly Lys Lys Leu Leu Pro Asp Asp Pro Tyr Glu Lys Ala Cys
 100 105 110
 Gln Lys Met Ile Leu Glu Leu Phe Ser Lys Val Pro Ser Leu Val Gly
 115 120 125
 Ser Phe Ile Arg Ser Gln Asn Lys Glu Asp Tyr Asp Gly Leu Lys Glu
 130 135 140
 Glu Phe Arg Lys Glu Phe Thr Lys Leu Glu Glu Val Leu Thr Asn Lys
 145 150 155 160
 Lys Thr Thr Phe Phe Gly Gly Asn Ser Ile Ser Met Ile Asp Tyr Leu
 165 170 175
 Ile Trp Pro Trp Phe Glu Arg Leu Glu Ala Met Lys Leu Asn Glu Cys
 180 185 190
 Val Asp His Thr Pro Lys Leu Lys Leu Trp Met Ala Ala Met Lys Glu
 195 200 205
 Asp Pro Thr Val Ser Ala Leu Leu Thr Ser Glu Lys Asp Trp Gln Gly
 210 215 220
 Phe Leu Glu Leu Tyr Leu Gln Asn Ser Pro Glu Ala Cys Asp Tyr Gly
 225 230 235 240
 Leu

<210> 205
 <211> 160
 <212> PRT
 <213> Homo sapien

<400> 205
 Met Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu
 1 5 10 15
 Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile Gln Asp
 20 25 30
 Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys
 35 40 45
 Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu
 50 55 60
 Ser Thr Leu His Leu Val Leu Arg Leu Arg Gly Gly Met Gln Ile Phe
 65 70 75 80
 Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser
 85 90 95
 Asp Thr Ile Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile
 100 105 110
 Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp
 115 120 125
 Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His
 130 135 140
 Leu Val Leu Arg Leu Arg Gly Gly Met Gln Ile Phe Val Lys Thr Leu
 145 150 155 160

<210> 206
 <211> 197
 <212> PRT
 <213> Homo sapien

<400> 206

Thr Ser Pro Ser Glu Ala Cys Ala Pro Leu Leu Ile Ser Leu Ser Thr
 1 5 10 15
 Leu Ile Tyr Asn Gly Ala Leu Pro Cys Gln Cys Asn Pro Gln Gly Ser
 20 25 30
 Leu Ser Ser Glu Cys Asn Pro His Gly Gly Gln Cys Leu Cys Lys Pro
 35 40 45
 Gly Val Val Gly Arg Arg Cys Asp Leu Cys Ala Pro Gly Tyr Tyr Gly
 50 55 60
 Phe Gly Pro Thr Gly Cys Gln Gly Ala Cys Leu Gly Cys Arg Asp His
 65 70 75 80
 Thr Gly Gly Glu His Cys Glu Arg Cys Ile Ala Gly Phe His Gly Asp
 85 90 95
 Pro Arg Leu Pro Tyr Gly Gly Gln Cys Arg Pro Cys Pro Cys Pro Glu
 100 105 110
 Gly Pro Gly Ser Gln Arg His Phe Ala Thr Ser Cys His Gln Asp Glu
 115 120 125
 Tyr Ser Gln Gln Ile Val Cys His Cys Arg Ala Gly Tyr Thr Gly Leu
 130 135 140
 Arg Cys Glu Ala Cys Ala Pro Gly His Phe Gly Asp Pro Ser Arg Pro
 145 150 155 160
 Gly Gly Arg Cys Gln Leu Cys Glu Cys Ser Gly Asn Ile Asp Pro Met
 165 170 175
 Asp Pro Asp Ala Cys Asp Pro His Thr Gly Gln Cys Leu Arg Cys Leu
 180 185 190
 His His Thr Glu Gly
 195

<210> 207

<211> 175

<212> PRT

<213> Homo sapien

<400> 207

Ile Ile Arg Gln Gln Gly Leu Ala Ser Tyr Asp Tyr Val Arg Arg Arg
 1 5 10 15
 Leu Thr Ala Glu Asp Leu Phe Glu Ala Arg Ile Ile Ser Leu Glu Thr
 20 25 30
 Tyr Asn Leu Leu Arg Glu Gly Thr Arg Ser Leu Arg Glu Ala Leu Glu
 35 40 45
 Ala Glu Ser Ala Trp Cys Tyr Leu Tyr Gly Thr Gly Ser Val Ala Gly
 50 55 60
 Val Tyr Leu Pro Gly Ser Arg Gln Thr Leu Ser Ile Tyr Gln Ala Leu
 65 70 75 80
 Lys Lys Gly Leu Leu Ser Ala Glu Val Ala Arg Leu Leu Glu Ala
 85 90 95
 Gln Ala Ala Thr Gly Phe Leu Leu Asp Pro Val Lys Gly Glu Arg Leu
 100 105 110
 Thr Val Asp Glu Ala Val Arg Lys Gly Leu Val Gly Pro Glu Leu His
 115 120 125
 Asp Arg Leu Leu Ser Ala Glu Arg Ala Val Thr Gly Tyr Arg Asp Pro
 130 135 140
 Tyr Thr Glu Gln Thr Ile Ser Leu Phe Gln Ala Met Lys Lys Glu Leu
 145 150 155 160
 Ile Pro Thr Glu Glu Ala Leu Arg Leu Trp Met Pro Ser Trp Pro

109

165

170

175

<210> 208

<211> 177

<212> PRT

<213> Homo sapien

<400> 208

Met Ala Ala Gly Val Glu Ala Ala Ala Glu Val Ala Ala Thr Glu Ile
 1 5 10 15
 Lys Met Glu Glu Glu Ser Gly Ala Pro Gly Val Pro Ser Gly Asn Gly
 20 25 30
 Ala Pro Gly Pro Lys Gly Glu Gly Glu Arg Pro Ala Gln Asn Glu Lys
 35 40 45
 Arg Lys Glu Lys Asn Ile Lys Arg Gly Gly Asn Arg Phe Glu Pro Tyr
 50 55 60
 Ala Asn Pro Thr Lys Arg Tyr Arg Ala Phe Ile Thr Asn Ile Pro Phe
 65 70 75 80
 Asp Val Lys Trp Gln Ser Leu Lys Asp Leu Val Lys Glu Lys Val Gly
 85 90 95
 Glu Val Thr Tyr Val Glu Leu Leu Met Asp Ala Glu Gly Lys Ser Arg
 100 105 110
 Gly Cys Ala Val Val Glu Phe Lys Met Glu Glu Ser Met Lys Lys Ala
 115 120 125
 Ala Glu Val Leu Asn Lys His Ser Leu Ser Gly Arg Pro Leu Lys Val
 130 135 140
 Lys Glu Asp Pro Asp Gly Glu His Ala Arg Arg Ala Met Gln Lys Val
 145 150 155 160
 Met Ala Thr Thr Gly Gly Met Gly Met Gly Pro Gly Gly Pro Gly Met
 165 170 175
 Ile

<210> 209

<211> 196

<212> PRT

<213> Homo sapien

<400> 209

Asp Leu Gln Asp Met Phe Ile Val His Thr Ile Glu Glu Ile Glu Gly
 1 5 10 15
 Leu Ile Ser Ala His Asp Gln Phe Lys Ser Thr Leu Pro Asp Ala Asp
 20 25 30
 Arg Glu Arg Glu Ala Ile Leu Ala Ile His Lys Glu Ala Gln Arg Ile
 35 40 45
 Ala Glu Ser Asn His Ile Lys Leu Ser Gly Ser Asn Pro Tyr Thr Thr
 50 55 60
 Val Thr Pro Gln Ile Ile Asn Ser Lys Trp Glu Lys Val Gln Gln Leu
 65 70 75 80
 Val Pro Lys Arg Asp His Ala Leu Leu Glu Glu Gln Ser Lys Gln Gln
 85 90 95
 Ser Asn Glu His Leu Arg Arg Gln Phe Ala Ser Gln Ala Asn Val Val
 100 105 110
 Gly Pro Trp Ile Gln Thr Lys Met Glu Glu Ile Gly Arg Ile Ser Ile
 115 120 125

Glu Met Asn Gly Thr Leu Glu Asp Gln Leu Ser His Leu Lys Gln Tyr
 130 135 140
 Glu Arg Ser Ile Val Asp Tyr Lys Pro Asn Leu Asp Leu Leu Glu Gln
 145 150 155 160
 Gln His Gln Leu Ile Gln Glu Ala Leu Ile Phe Asp Asn Lys His Thr
 165 170 175
 Asn Tyr Thr Met Glu His Ile Arg Val Gly Trp Glu Gln Leu Leu Thr
 180 185 190
 Thr Ile Ala Arg
 195

<210> 210
 <211> 156
 <212> PRT
 <213> Homo sapien

<400> 210
 Lys Leu Thr Ile Glu Ser Thr Pro Phe Asn Val Ala Glu Gly Lys Glu
 1 5 10 15
 Val Leu Leu Leu Ala His Asn Leu Pro Gln Asn Arg Ile Gly Tyr Ser
 20 25 30
 Trp Tyr Lys Gly Glu Arg Val Asp Gly Asn Ser Leu Ile Val Gly Tyr
 35 40 45
 Val Ile Gly Thr Gln Gln Ala Thr Pro Gly Pro Ala Tyr Ser Gly Arg
 50 55 60
 Glu Thr Ile Tyr Pro Asn Ala Ser Leu Leu Ile Gln Asn Val Thr Gln
 65 70 75 80
 Asn Asp Thr Gly Phe Tyr Thr Leu Gln Val Ile Lys Ser Asp Leu Val
 85 90 95
 Asn Glu Glu Ala Thr Gly Gln Phe His Val Tyr Pro Glu Leu Pro Lys
 100 105 110
 Pro Ser Ile Ser Ser Asn Asn Ser Asn Pro Val Glu Asp Lys Asp Ala
 115 120 125
 Val Ala Phe Thr Cys Glu Pro Glu Val Gln Asn Thr Thr Tyr Leu Trp
 130 135 140
 Trp Val Asn Gly Gln Ser Leu Pro Val Ser Pro Lys
 145 150 155

<210> 211
 <211> 92
 <212> PRT
 <213> Homo sapien

<400> 211
 Met Glu Ser Pro Ser Ala Pro Pro His Arg Trp Cys Ile Pro Trp Gln
 1 5 10 15
 Arg Leu Leu Leu Thr Ala Ser Leu Leu Thr Phe Trp Asn Pro Pro Thr
 20 25 30
 Thr Ala Lys Leu Thr Ile Glu Ser Thr Pro Phe Asn Val Ala Glu Gly
 35 40 45
 Lys Glu Val Leu Leu Leu Val His Asn Leu Pro Gln His Leu Phe Gly
 50 55 60
 Tyr Ser Trp Tyr Lys Gly Glu Arg Val Asp Gly Asn Arg Gln Ile Ile
 65 70 75 80
 Gly Tyr Val Ile Gly Thr Gln Gln Ala Thr Pro Gly

85

90

<210> 212
 <211> 142
 <212> PRT
 <213> Homo sapien

<400> 212

Glu Lys Gln Lys Asn Lys Glu Phe Ser Gln Thr Leu Glu Asn Glu Lys
 1 5 10 15
 Asn Thr Leu Leu Ser Gln Ile Ser Thr Lys Asp Gly Glu Leu Lys Met
 20 25 30
 Leu Gln Glu Glu Val Thr Lys Met Asn Leu Leu Asn Gln Gln Ile Gln
 35 40 45
 Glu Glu Leu Ser Arg Val Thr Lys Leu Lys Glu Thr Ala Glu Glu Glu
 50 55 60
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 65 70 75 80
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 Asp Lys Ile Leu Gly Ala Thr Ile Glu Asn Ser Arg Ile Val Leu Gln
 85 90 95
 Ile Asp Asn Ala Arg Leu Ala Ala Asp Asp Phe Arg Thr Lys Phe Glu
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      50           55           60
Glu Leu Arg Ser Leu Leu Gly Lys Asp Val Leu Phe Leu Lys Asp Cys
      65           70           75           80
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<213> Homo sapien

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      35           40           45
Leu Ala Leu Val Asp Val Leu Glu Asp Lys Leu Lys Gly Glu Met Met
      50           55           60
Asp Leu Gln His Gly Ser Leu Phe Leu Gln Thr Pro Lys Ile Val Ala
      65           70           75           80
Asp Lys Asp Tyr Ser Val Thr Ala Asn Ser Lys Ile Val Val Val Thr
      85           90           95
Ala Gly Val Arg Gln Gln Glu Gly Glu Ser Arg Leu Asn Leu Val Gln
      100          105          110
Arg Asn Val Asn Val Phe Lys Phe Ile Ile Pro Gln Ile Val Lys Tyr
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Thr Tyr Val Thr
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<213> Homo sapien

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 85 90 95
 Trp Glu Lys Thr Pro Glu Ser Trp Gly Pro Ala Pro Thr Ile Gly Glu
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 Ala Pro Lys Asn Gly Thr Leu Glu Pro Gly Thr Glu Arg Arg Ala Pro
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 Gly Pro Gly Ser Gly Val Asp Ala Lys Ala Gly Trp Val Asp Asn Thr
 195 200 205
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 Pro Arg Arg Leu Glu Pro Ala Pro Pro Arg Ala Arg Pro Glu Val Ala
 225 230 235 240
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 245 250 255
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 290 295 300
 Leu Thr Leu Thr Pro Phe Pro Gly Pro Gly Pro Arg Arg Pro Pro Trp
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 325 330 335
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 340 345 350
 Glu Glu Asp Glu Glu Ala Ala Ala Pro Gly Ala Ala Ala Gly Pro Arg
 355 360 365
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 370 375 380
 Ala Asp Ala Asp Ala Ala Arg Pro Leu Arg Gly Leu Leu Lys Ser Pro
 385 390 395 400
 Arg Gly Ala Asp Glu Pro Glu Asp Ser Glu Leu Glu Arg Lys Arg Lys
 405 410 415
 Met Val Ser Phe His Gly Asp Val Thr Val Tyr Leu Phe Asp Gln Glu
 420 425 430
 Thr Pro Thr Asn Glu Leu Ser Val Gln Ala Pro Pro Glu Gly Asp Thr

435 440 445
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450 455 460
Pro Gly Asp Gly Phe Pro Ser Asn Asp Ser Gly Phe Gly Gly Ser Phe
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Glu Trp Ala Glu Asp Phe Pro Leu Leu Pro Pro Gly Pro Pro Leu
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515 520 525

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US99/01642

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(71) Applicant: CORIXA CORPORATION [US/US]; Suite 200,
1124 Columbia Street, Seattle, WA 98104 (US).(72) Inventors: REED, Steven, G.; 2843 - 122nd Place N.E.,
Bellevue, WA 98005 (US). LODES, Michael, J.; 9223 -
36th Avenue S.W., Seattle, WA 98126 (US). FRUDAKIS,
Tony, N.; P.O. Box 99232, Seattle, WA 99232-0232 (US).
MOHAMATH, Raodoh; 4205 South Morgan, Seattle, WA
98118 (US).(74) Agents: MAKI, David, J. et al.; Seed and Berry LLP,
6300 Columbia Center, 701 Fifth Avenue, Seattle, WA
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LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,
MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent
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(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent
(AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT,
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and to be republished in the event of the receipt of amendments.*(88) Date of publication of the international search report:
9 December 1999 (09.12.99)

(54) Title: COMPOUNDS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER AND METHODS FOR THEIR USE

(57) Abstract

Compounds and methods for treating lung cancer are provided. The inventive compounds include polypeptides containing at least a portion of a lung tumor protein. Vaccines and pharmaceutical compositions for immunotherapy of lung cancer comprising such polypeptides, or polynucleotides encoding such polypeptides, are also provided, together with polynucleotides for preparing the inventive polypeptides.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/01642

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/12 A61K38/17 C07K14/47 C07K16/18 A61K35/14

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C12Q A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 96 30389 A (MILLENIUM PHARMACEUTICALS, INC.; SHYJAN A.) 3 October 1996 see page 112 - page 127 ---	1-60
A	WO 96 02552 A (CYTOCLONYL PHARMACEUTICS, INC.; TORCZYNSKI R. ET AL.) 1 February 1996 see the whole document ---	1-60
A	YOU L ET AL.: "Identification of early growth response gene-1 (Egr-1) as a phorbol myristate-induced gene in lung cancer cells by differential mRNA display" AM. J. RESPIR. CELL MOL. BIOL., vol. 17, no. 5, November 1997, pages 617-624, XP002106654 see page 618, left-hand column, paragraph 3 --- -/--	1,2,4-7

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

21 June 1999

Date of mailing of the international search report

22 10. 1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

CUPIDO, M

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/01642

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>CHEN S-L ET AL: "Isolation and characterization of a novel gene expressed in multiple cancers" ONCOGENE, vol. 12, no. 4, 15 February 1996, pages 741-751, XP002106655 see page 741, right-hand column, last paragraph - page 743 -----</p>	1,2,4-7

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/ 01642

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 16, 17, 24-26, 32, 33, 48-53 and 56-58 are directed to a method of treatment of the human/animal body the search has been carried out and based on the alleged effects of the composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see FURTHER INFORMATION sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
see FURTHER INFORMATION sheet, subject 1.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/ US 99/01642

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: Claims 1,2,4-12,16-25 and 27-60 (all partly and as far as applicable):

Polynucleotides comprising the sequence provided in SEQ ID NO:1, their corresponding complement sequences, variants thereof, polypeptides, vectors, pharmaceutical compositions, pharmaceutical compositions for the treatment of lung cancer, vaccines, applications thereof, fusion proteins, diagnostics, monoclonal antibodies and T cells or antigen presenting cells incubated in the presence of said polynucleotides or polypeptides.

Inventions 2-128: Claims 1-60 (all partly and as far as applicable):

Idem as invention 1 but limited to each of the DNA sequences as in SEQ ID NO: 2-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120, 126-181 and as far as applicable.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/01642

PLT/US 99/01642

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9630389	A	03-10-1996	US 5633161 A	27-05-1997
			AU 708746 B	12-08-1999
			AU 5437896 A	16-10-1996
			CA 2216717 A	03-10-1996
			EP 0817792 A	14-01-1998
			US 5674739 A	07-10-1997

WO 9602552	A	01-02-1996	US 5589579 A	31-12-1996
			AU 700915 B	14-01-1999
			AU 3359295 A	16-02-1996
			BR 9508417 A	18-11-1997
			CA 2195403 A	01-02-1996
			EP 0804451 A	05-11-1997
			JP 10503087 T	24-03-1998
			US 5773579 A	30-06-1998

Form PCT/ISA/210 (patent family annex) (July 1992)

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